BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 28.] 1931. [No. 11.

PLAGUE.

ESKEY (C. R.). **Chief Etiological Factors of Plague in Ecuador and the Antiplague Campaign.**—*Public Health Rep.* 1930. Sept. 5 & 12. Vol. 45. Nos. 36 & 37. pp. 2077–2115; 2162-2187. With 7 figs. on 2 plates, 1 map & 1 chart.

From this account we learn that Peru was the first country on the west coast of South America to be invaded by plague, the infection having been brought to it from India in 1903 by a ship with a cargo of jute-bags. The infection reached Ecuador, the adjoining country to the north of Peru, by sea through the port of Guayaquil; in February, 1908, a severe epizootic broke out among the rats in this town. The epizootic in Guayaquil was followed soon afterwards by human plague; there were 63 cases in February 1908 and 225 cases in March—the greatest number reported here in a single month. During the 22 years from 1908 to 1930, 7,616 cases were notified in Guayaquil, and an analysis of their distribution shows that there has been a decline in each successive period of five years, apparently attributable to an increasing immunity among the rat population.

Prior to 1916 the epidemic reached its peak in October–December, the last months of the dry season, but in later years most of the cases occurred in January–March, the first three months of the rainy season. The explanation seems to lie in the difference in susceptibility of the house-rats and outdoor rats. The former have acquired a considerable immunity to plague, whereas the outdoor rats, owing to their low *cheopis* infestation are more susceptible. Consequently when the floods during the rainy season cause these rats to seek shelter within buildings the epizootic increases, and in its wake the epidemic.

From this port the infection spreads to the lowland towns and to the towns in the mountains by the transport of rats in the rolling stock of the Guayaquil–Quito railway. In Ecuador plague is found at altitudes of over 10,000 feet above sea-level. Guayaquil is considered to be the endemic source of plague in the country, and especially the quarter of the town which contains many wooden buildings with double floors and party-walls; these afford excellent harbourage for rats. In the mountainous districts the conditions and habits of

(19954) Wt P5/68 1,875 11/31 H & Sp Gp 52

life of the Indians favour the spread of plague ; there is one living-room and often an adjoining room for the storage of grain. Guineapigs appear to be the favourite domesticated animal ; often 20 or more of them run free in the living-room. Their flesh is greatly relished and is the chief item of food at the *fiestas*. The close association of these animals with man is the source of many plague cases, and although the breeding of guineapigs in houses is prohibited, the law is not enforced. The " velorio," or death-wake, is an Indian custom which helps to spread plague. The relatives and friends come from long distances to the ceremony, which lasts from 2 to 5 days ; they feast, drink, and lie about the room of the deceased in a drunken stupor most of the time ; and they handle the body and clothing of the dead person. When the company return to their houses some of them may be incubating the disease and may be carrying infected fleas.

In Ecuador bubonic plague is the commonest form and axillary buboes are said to be often seen, especially in the mountainous districts [an observation which suggests to the reviewer a causal connexion with the use of guineapigs as food] ; many similar examples in the recent history of plague illustrate the danger of infecting abrasions or cuts on the hand when skinning animals for food or for the sale of their fur. Exact statistics of the type of plague are not available, but septicaemic plague is not likely to be common because of the generally low death-rate. Pneumonic plague is said to be rare. Two unusual forms of plague occur : (1) tonsillar plague, angina pestosa, and (2) " viruela pestosa," a form resembling chicken-pox or smallpox ; these forms are especially seen in the mountainous regions. The anginal form results from the habit of the Indians of killing vermin—*P. irritans* or lice—with their teeth. The cutaneous variety begins as bubonic plague and the skin eruption passes through stages which are very like those of chicken-pox. These types are more fatal than the ordinary bubonic form. The general mortality-rate is unusually low, about 37 per cent., and this figure is probably an over-estimate owing to the omission of unreported cases that recover.

In Guayaquil from 75 to 80 per cent. of the rats trapped are *R. norvegicus*, and the remaining rats are *R. rattus*. About 60 per cent. of the rodents trapped are mice. The detection of plague in the rats of this town is difficult, because they do not present the appearances that have been noted in other parts of the world to be characteristic of rat-plague.

X. cheopis is the species of flea which is chiefly concerned in the spread of plague in Ecuador, and it is the only species which transmits rat-plague. This flea is found at an altitude of over 9,000 feet, but not in sufficient numbers to maintain plague in epidemic form. The highest altitude at which *X. cheopis* plays an effective part as a plague carrier is about 8,500 feet. *R. rattus* has a higher *cheopis* index than *R. norvegicus*. *X. cheopis* is found in such scanty numbers on mice as to deprive them of power to transmit plague. Quito, a town of 100,000 inhabitants, at the terminus of the Guayaquil and Quito railway, 9,350 feet above sea-level, has never had a case of plague, for the reason that the conditions are not favourable for the reproduction of *X. cheopis* in numbers adequate to bring about a rodent epidemic.

Ceratophyllus londinensis is found on rats and mice at an altitude of over 8,000 feet, but it is not important as a plague carrier. *Leptopsylla musculi* is found on rats and mice in all the towns in the mountains, but, as elsewhere, is of no importance in the spread of plague ; it is

the commonest rodent flea at Quito, a plague-free town. In Ecuador *Rhopalopsyllus cavicola* infests guineapigs and is found in great numbers in the mountainous districts, even at an elevation of 10,000 feet; large numbers can be found at Quito. This flea does not seem to bite man and is probably not an active transmitter of plague.

P. irritans abounds everywhere and is one of the pests of Ecuador. The author gives reasons for his belief that this species is the chief transmitter of plague to man in localities where no *X. cheopis* are found. [The reviewer has recently summarized the evidence bearing on the rôle of the human flea in plague, and is sceptical of its importance.* In his opinion the rarity of septicaemic cases in Ecuador still further reduces the probability that *P. irritans* possesses significance in this connexion.]

On account of financial stringency, radical measures for the prevention of plague, such as ratproofing buildings, cannot be applied, and as a substitute a poisoning campaign has been organized in Guayaquil. The author of the Report concludes that the use of poison is a safe, simple, effective and inexpensive procedure. He regards a reduction of 80 per cent. in the incidence of plague in January–March 1930, by this method, as a conservative estimate; the coincident trapping was a minor factor in producing the result. He believes that if the measures he describes are continued they may eradicate plague from Guayaquil, and in consequence bring about the disappearance of the disease in Central Ecuador; but the description of the unhygienic conditions which favour rat infestation in Guayaquil may arouse doubts in the reader's mind. Poison baits which contain either barium carbonate or arsenic are used. The most effective is believed to be a mixture of dried codfish, corn-meal and arsenic. The poison-mixtures are changed from time to time. Oil of anise is used to scent the baits and seems to attract rats, but not other animals.

The observations collected by the author are summarized in 43 tables appended to the Report.

G. F. Petrie.

MOREAU. Note sur le service médical du lazaret de Saint-Louis (Sénégal) pendant l'épidémie de peste de 1929. [**Plague in Senegal, 1929.**]—*Ann. de Méd. et de Pharm. Colon.* 1930. Apr.-May-June. Vol. 28. No. 2. pp. 218–235.

The author describes an outbreak of plague from May to October 1929. The aspects of the disease were of the usual nature. Of 289 cases treated, 122 died. There were 4 cases of pulmonary plague, all fatal. Out of the 289 attacked, 234 had been vaccinated with an anti-plague lipo-vaccine on dates shown on their cards, 32 were stated to have been vaccinated, but there were no cards to prove the statements; 23 had never been vaccinated. There were 94 deaths among those properly vaccinated. The value of serum treatment is recognized by the author, but he concludes that the value of serotherapy depends on its administration at the earliest possible moment. 200 cc. was given to adults daily.

J. H. Tull Walsh.

* MEDICAL RESEARCH COUNCIL. A System of Bacteriology in Relation to Medicine. Vol. 3. p. 184. (1929. London: H.M. Stationery Office.)

DANY (Henri). La peste dans le Sous. Historique. La vaccination et les autres procédés de lutte. [**Plague in Sous, Morocco.**]—*Rev. Méd. et Hyg. Trop.* 1931. May-June. Vol. 23. No. 3 pp. 113–126. With 1 map. [3 refs.]

This is the second paper referring to the 1929 epidemic. It deals with the topographical history of the outbreak, anti-plague vaccination and the general methods employed for checking the infection. There seem to have been two centres of origin, one in Ait Amira and another in Ait Amer-Ait Milk from which the disease spread partly due to rats and possibly in part due to man. The good effect of anti-plague vaccination is admitted, but its value for immunity is of short duration. The medical staff and assistants in plague hospitals were vaccinated with anti-plague serum plus anti-plague vaccine and no case of plague occurred among those persons. For destruction of rats the Danysz virus gave good results [*ante*, p. 381 (DANY)].

J. H. T. W.

NATTAN-LARRIER (L.) & RICHARD (L.). Les lésions histologiques de la peste pulmonaire primitive. [**Histology of Primary Pneumonic Plague.**]—*Bull. Soc. Path. Exot.* 1931. May 13. Vol. 24. No. 5. pp. 388–394. [3 refs.]

The authors state that their results differ somewhat from those described from pneumonic plague in Manchuria. The specimens they examined came from Madagascar. The lesions as observed by them are those of lobular bronchopneumonia where the alveoli filled with bacteria are mixed irregularly with catarrhal alveoli; they insist on the frequency of phagocytosis and have not found the grave lesions in the small pulmonary vessels described by other writers; nor have they seen thromboses and diffuse haemorrhages with rupture of the alveolar walls as described by SIGNORELLI, WU-LIEN-TEH and CHENZINSKI. Their own findings are discussed and compared with those of previous workers. They admit that they do not know at what period of the epidemic their specimens were collected, nor do they know how long the disease had lasted before death supervened.

J. H. T. W.

JOLTRAIN. Pestes frustes et ambulatoires. [**Aborted and Ambulatory Plague.**]—*Bull. Acad. Royale de Méd. Belgique.* 1930. Oct. 25. Ser. 5. Vol. 10. No. 9. pp. 663–677.

The author recalls the appearance of plague in the neighbourhood of Paris in 1920 after a period of freedom from the disease for nearly three centuries [this *Bulletin*, Vol. 20, p. 362 (JOLTRAIN)]. For the past ten years the author has been studying these early cases in their epidemiological, clinical and diagnostic aspects. He quotes certain cases and refers especially to abortive and ambulatory cases of bubonic plague which were relatively frequent. Similar cases occurred during following years and a certain number of infected rats were discovered. Clinically these cases present general febrile symptoms with a bubo. When this suppurates the temperature falls and the patient recovers. The diagnosis is difficult and the discovery of the bacillus often impossible. In one case mentioned *Bact. tularense* was suspected. Serum

from the patient was sent to the Lister Institute. The report stated that agglutination with *Bact. tularense* was negative. Cases of abortive and ambulatory plague are stated to be fairly frequent in Algeria where plague is endemic.

J. H. T. W.

LEMAIRE (G.) & BARDENAT (E.). Quelques complications rares au cours de la peste bubonique (Alger 1930). [**Rare Complications in Bubonic Plague, Algiers.**]—*Bull. Soc. Path. Exot.* 1931. Apr. 15. Vol. 24. No. 4. pp. 274–279.

These observations were made in Algiers during the year 1930. The first complication referred to is secondary pneumonia with bloody sputum in severe cases of bubonic plague. Such cases are not always fatal as is generally the case in primary pneumonic plague. Sometimes the softness of the bubo was not due to suppuration; only a grey serous fluid was obtained and on incision the bubo showed a caseous mass, grey or even black. Two cases are described in detail in which the eyes were implicated showing iritis and hypopyon. Both these patients died.

J. H. T. W.

i. FONQUERNIE (J.). Observations sur un cas de Pestis minor. [**A Case of Pestis minor.**]—*Bull. Soc. Path. Exot.* 1931. June 10. Vol. 24. No. 6. pp. 446–448. [Municipal Bureau of Hyg., Antananarivo.]

ii. LEGER (Marcel). A propos de la communication de Fonquernie sur des cas de Pestis minor. [**Remarks on the above.**]—*Ibid.* pp. 448–450.

i. On the 27th January, 1931, Rainijaona, aged 75, died of septicaemic plague after two days' illness. In the house in which he lived and in the three adjacent houses there had not been any case of plague since 1927. In that year Rainijaona's wife died of plague and there were four other cases in that group of houses. On January 28th, 1931, Razafindrakoto, aged 9, a servant in the house of the deceased man, was taken into the plague hospital. It was stated that he had been ill eight days. When seen on the 28th there was a large bubo in the right axilla; temperature normal. The bubo was punctured on the 29th and the fluid sent to the Pasteur Institute. *Past. pestis* was found and cultivated. The temperature remained normal except for a trifling rise of 0·6° two days after incision of the bubo.

ii. Leger considers the case reported by M. Fonquernie both interesting and important. It suggests the conservation of the virus in one area for a long period. It recalls to his mind cases of mild and aborted ambulatory plague during epidemics in Dakar during 1921, 1922 and 1923. These cases were sometimes fatal.

J. H. T. W.

RASOAMANANA (G.). Sur un cas d'angine pesteuse avec présence d'un bubon sus-claviculaire. [**Plague Angina with Bubo above the Clavicle.**]—*Bull. Soc. Path. Exot.* 1931. Feb. 11. Vol. 24. No. 2. pp. 164–166.

The author describes the case of a missionary, a native of Madagascar, who had suffered from sore throat for 48 hours. The throat was much inflamed and there was a painful gland just above the left clavicle. In

spite of treatment with anti-plague serum the patient died 12 hours after admission to hospital. Smears from the throat and fluid from the bubo showed the bacillus of Yersin. Smears taken from the body after death showed plague bacilli in the lungs and liver.

J. H. T. W.

ACCOYER (H.). Relation de quelques cas de peste observés à Beyrouth. [**Plague in Beirut.**]—*Arch. Méd. et Pharm. Milit.* 1931. Mar. Vol. 94. No. 3. pp. 470–474.

Plague is not often seen in Beirut, but from time to time sporadic cases occur confined as a rule to persons occupied in the traffic of the port. The infection seems to come from Egypt. Four cases occurring in 1923 and two in 1929 are described in detail. Of the first cases two recovered, and in 1929 one of the cases recovered.

J. H. T. W.

DURAND (Paul). Un cas de peste chronique ayant duré 17 mois. [**Chronic Plague of 17 Months Duration.**]—*Arch. Inst. Pasteur de Tunis.* 1931. Apr. Vol. 20. No. 1. pp. 77–82. [3 refs.]

The author writes that while no doubt rats are the chief reservoir and source of plague it becomes more and more evident that man and his fleas may become an agent in spreading the infection. He describes in detail a case observed in 1929 in the Rabta plague hospital. The essential fact is that a man suffering from bubonic plague contained in his body for seventeen months plague bacilli which were lethal to a guineapig. References are given to papers bearing on this matter. [See this *Bulletin*, Vol. 24, p. 933 (NIKANOROW) ; p. 934 (DURAND & CONSEIL).]

J. H. T. W.

LINDBERG (K.). Deux cas de peste bubonique traités par le sérum et le mercurochrome. [**Bubonic Plague treated with Serum and Mercurochrome.**]—*Rev. Méd. et Hyg. Trop.* 1931. May-June. Vol. 23. No. 3. pp. 149–152.

During the winter of 1930 when plague was prevalent in the Bombay Presidency the author was able to keep two cases under observation. Both these cases were treated with anti-plague serum injections and each received intravenous injections of 20 cc. of a 1 per cent. solution of mercurochrome. The cases are described in detail. Both recovered, and as regards the treatment the author writes that without doubt anti-plague serum given from the beginning of the disease was of value in both cases. It is difficult to say whether the mercurochrome had any influence, one way or another, on the results in the first case, but in the second case, a very severe one, it appeared that the doses of mercurochrome did produce a marked effect. [See this *Bulletin*, Vol. 25, p. 319 ; and Vol. 27, p. 734 (CAIUS, KAMAT, NAIDU).]

J. H. T. W.

VINCENT (G. W.). **Four Cases of Plague treated with "Bayer 205."**—*Indian Med. Gaz.* 1931. Mar. Vol. 66. No. 3. pp. 126–127.

During a severe epidemic of plague in Maymyo (Burma), August, 1927, the author treated four cases of plague successfully with intravenous injections of "Bayer 205." The cases are described in detail. One was a Hindu lady 54 years of age, the others were boys 5, 7 and 14 years old.

J. H. T. W.

GOUBAREV (E.) & LIPATOVA (T.). Influence de certains anions et cations sur le développement des B. pesteux. [**Influence of Certain Anions and Cations on** *Past. pestis*.]—*Rev. Microbiol, Epidémiol. et Parasit.* 1930. Vol. 9. No. 4. pp. 507–512. [5 refs.] [In Russian. French summary.] [Inst. of Microbiol & Epidemiol., Saratov.]

In these experiments on the influence of certain anions and cations on the development of *Past. pestis* a definite number of bacilli from 48-hour cultures were placed in a series of tubes containing broth diluted 1 : 1, with a certain concentration of the salt. The control tubes contained the same quantity of broth diluted with distilled water. The tubes were placed in an incubator at 28° C. After 48 hours a fixed quantity of bacilli was taken from each tube and sown on agar on Petri dishes. The colonies were counted after 48 hours: NaCl at a concentration of 16 parts per thousand (excluding the 0·5 in the medium) shows an inhibitive action and KCl checks growth more strongly than NaCl. NH_4Cl in concentration less than 16·6 stimulates development. BaCl favours development (1·66); but $CaCl_2$ and $SrCl_2$ (8·3) check growth. At 8·3 $MnCl_2$ stimulates growth as does Na_2SO_4. $CuCl_2$, 1·66, and NaI, 0·83 parts, check development.

J. H. T. W.

i. GAISKY (N.). Un nouveau porteur de peste—*Ellobius talpinus* Pall. [**A New Carrier of Plague.**]—*Rev. Microbiol., Epidémiol. et Parasit.* 1931. Vol. 10. No. 1. pp. 59–61. With 1 text fig. [In Russian. French summary p. 61.]

ii. POPOW (W.). Zur Frage ueber die *B. pestis*-Lokalisation in Organen der Zieseln bei spontaner Pest. [**Localization of** *Past. pestis* **in Marmots.**]—*Ibid.* pp. 63–67. [5 refs.] [In Russian. German summary p. 68.]

i. During an epizootic among spermophiles in 1928 in the Urals mortality was observed of *Ellobius talpinus*. Two of these animals were examined and cultures of *Past. pestis* were obtained. Ninety per cent. of the fleas found on Ellobius are *Xenopsylla mycerini*. Sometimes *Cer. tesquorum*, *Ct. breviatus* and *Ct. pollex* are found; more rarely still *Neopsylla setosa*. A tick, *Rhipicephalus schulzei*, was also found.

ii. The author states that the absence of gross pathological conditions does not exclude the presence of plague. Marmots, in good health, were taken from an area in which epizootics were present. Sections of the spleen, liver, lungs and glands and cultures, on agar, were made. Of 608 marmots 25 showed the plague bacillus, especially in the spleen and liver.

J. H. T. W.

LEVINTHAL (Walter). Schwierigkeiten der Pestdiagnose bei Schiffsratten. [**Difficulties of Diagnosis of Plague in Ship's Rats.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1931. May 22. Vol. 112. No. 3. pp. 433–435. [1 ref.] [Robert Koch Inst., Berlin.]

The author's difficulties are based upon the fact that the ship's rat contains *Past. pseudotuberculosis* as well as the plague bacillus and that there is no rapid and certain method for differentiating these bacilli. Both are Gram-negative, both bipolar and even culture reactions with

sugars and agglutinations reactions are not always reliable. The author does not offer any solution of the problem ; but expresses a hope that a bacterioscopic method will be found by which the plague bacillus may be quickly distinguished in the dead body of the rat. [See this *Bulletin*, Vol. 26, p. 99 (ZLATOGOROFF) ; Vol. 27, p. 739 (BEZSONOVA, KOROBKOVA).]

J. H. T. W.

RUKKE (G. V.). **Rodent Destruction.**—*Milit. Surgeon.* 1930. Nov. Vol. 67. No. 5. pp. 592–599.

Bubonic plague infected ground squirrels are found throughout a great area of California. The infection is spreading and the possibility of spread to other susceptible animals and to other states is not a remote possibility. All prospective military movements should be preceded by an intensive survey and campaign against rodents including the ground squirrel. This campaign should be a sufficient time in advance so that the infected fleas left after the death of the hosts shall have disappeared. [See this *Bulletin*, Vol. 26, p. 634 (GESSNER).]

J. H. T. W.

GIRARD (G.). Immunité du Hérisson et du Tanrec à la peste expérimentale. [**Immunity of Hedgehog and Tenrec to Plague.**]—*C.R. Soc. Biol.* 1931. Apr. 24. Vol. 106. No. 12. pp. 1078–1080. [Pasteur Inst., Antananarivo.]

The author describes laboratory experiments on two Insectivores of Madagascar : a hedgehog, *Ericulus setosus* and the tenrec, *Centetes ecaudatus*. These animals do not naturally suffer from plague and were found entirely immune to inoculations with plague bacilli.

J. H. T. W.

FARMAKIDIS (C.). Quelques observations cliniques sur la peste.—*Rev. Prat. Malad. des Pays Chauds.* 1930. Oct. Year 9. Vol. 10. No. 10. pp. 475–477.

GEBEILI (E.). Quelques considérations sur la prophylaxis de la peste et la marche de la légère épidémie de 1929 à Alexandre.—*Rev. Prat. Malad. des Pays Chauds.* 1930. Oct. Year 9. Vol. 10. No. 10. pp. 482–486 ; 493–498.

KALINA (G. P.). " Aljau-Met " (" Allgemeines Elend ") und Pest an Murmeltieren (Marmota bobak) in Südkirgisien.—*Rev. Microbiol., Epidémiol. et Parasit.* 1930. Vol. 9. No. 4. pp. 549–552. [In Russian. German summary.]

MORRISON (A.). Sur la localisation des ganglions cruraux dans la peste.—*Rev. Prat. Malad. des Pays Chauds.* 1930. Oct. Year 9. Vol. 10. No. 10. pp. 478–481.

CHOLERA.

GILL (C. A.) & LAL (R. B.). **The Epidemiology of Cholera, with Special Reference to Transmission. A Preliminary Report.**—*Indian Jl. Med. Res.* 1931. Apr. Vol. 18. No. 4. pp. 1255–1297. With 3 charts & 1 map in text. [17 refs.]

In this preliminary report an opinion based on epidemiological evidence is presented, which would incriminate the housefly as an important transmitting agent of cholera. The main fact emerging from the experimental evidence is that isolation of a vibrio with the morphological characters of the cholera vibrio, giving a cholera red reaction, and agglutinating with cholera serum was effected from flies 4 or 5 days after feeding on cholera vibrio suspensions. This isolation followed on negative results of culture between the second and fourth day after feeding. A suggestion is, consequently, put forward that the vibrio may undergo development in the body of the fly. It is only advanced tentatively as the evidence pointing to the accuracy of the hypothesis is recognized by the authors to be meagre and to require further investigation.

W. F. Harvey.

D'HERELLE (F.). **Studies upon Asiatic Cholera.**—*Yale Jl. of Biol. & Med.* 1929. Mar. Vol. 1. No. 4. pp. 195–219. With 6 charts.

The introductory remarks contain a sound criticism of some purely laboratory work ; very rarely have these studies been made with fresh material at the bedside of the patient. Much of this laboratory work is done with old cultures from vibrios long separated from their natural environment. "And what shall we say of the results obtained by those who have undertaken to study the pathogenesis of cholera by animal inoculations, by attempting to infest with old strains of the vibrio guineapigs and rabbits, animals which are completely refractory ?"

The rest of the paper recapitulates the work done in India by d'Herelle, MALONE and LAHIRI, at the request of the Indian Government in 1927. [This *Bulletin*, Vol. 26, p. 86 (d'Herelle) ; Vol. 27, p. 602 and pp. 1026–1027 (d'Herelle, MALONE, LAHIRI).]

J. H. Tull Walsh.

i. WU LIEN-TEH. **Preliminary Report upon Cholera Investigations in Shanghai, Summer 1930.**—*Publications National Quarantine Service, Republic of China.* 1931. Feb. 10. Ser. I. pp. 1–57. With 1 diagram. [Refs. in footnotes.]

ii. GAUTIER (R.). **Epidemiological Study of Cholera in Shanghai.**—*Malayan Med. Jl.* 1931. Mar. Vol. 6. No. 1. pp. 1–6.

i. The National Quarantine service of China was established on July 1st, 1930, and the port health work of Shanghai was taken over from the Commissioner of Customs. At the same time the fumigating vessels *Jennie* and *Jessie* passed into the hands of the Quarantine Service. With the help of Dr. C. L. PARK (Chief of the Epidemiological Division of the League of Nations (Health Section), a new set of Quarantine Regulations was published. When an outbreak of cholera occurred, late in the summer, the authorities were ready to fight it,

with the result that only 128 cases were recorded, with 16 deaths. 537,034 anti-cholera vaccinations, done since May 15th, contributed not a little to this satisfactory result. The Chinese Hygienic Laboratory prepared one million doses for distribution in 1931. The Report contains an account of the scope and method of investigation with many tables. It also contains a Report on the Quarantine needs of Shanghai by Dr. C. L. PARK. Dr. Wu Lien-Teh's remarks on vibrios closely cholera-like which do not agglutinate are of interest :

" Some investigators not only believe that such vibrios are identical with the *V. cholera* but that they can again become agglutinable. Tempting as such an assumption is, one hesitates to accept it as it may involve belief in the indigenous origin of cholera in various parts of the world . . . . . We have observed a number of instances where true cholera vibrios lost their agglutinability under our own eyes and stated our belief that the strains, found non-agglutinating from the first, may have undergone a similar involution before they reached us. In other words, there might have been a period in their history when they were agglutinable and probably virulent as well . . . ." [See TOMB & MAITRA, this *Bulletin*, Vol. 24, p. 460 ; Vol. 27, p. 14. BRAHMACHARI, Vol. 25, p. 305 ; Vol. 27, pp. 19 ; 858.]

ii. This is quite an interesting paper on cholera and the epidemiological conditions in Shanghai. The author remarks that the bacteriophage offers at the present time one of the most controversial but at the same time possibly promising fields of research in connexion with cholera.

J. H. T. W.

SHAHA (B.). **Shock in Cholera.**—*Med. Rev. of Reviews.* 1931. Jan. Vol. 6. No. 1. pp. 1–3.

The author refers to certain cases of cholera allied to what is known as *cholera sicea.* Severe cholera can occur without raising the specific gravity of the blood. It causes therefore a state of shock. This condition can only be made out by routine blood specific gravity tabling before giving saline injections. Intravenous saline injections cannot be freely used in such cases for fear of pulmonary oedema. Normal saline by the subcutaneous method and hypotonic saline by rectal injection are useful with general treatment for shock.

J. H. T. W.

ASHESHOV (Ignor N.), KHAN (Saranjam) & LAHIRI (M. N.). **The Treatment of Cholera with Bacteriophage.**—*Indian Med. Gaz.* 1931. Apr. Vol. 66. No. 4. pp. 179–184. [Bacteriophage Enquiry, Indian Research Fund Assoc., Bankipore, B. & O.]

That this treatment has roused the enthusiasm of the authors to a high pitch is evident and may be illustrated by their own statements that : " We could hardly believe our own results . . . . The mortality from cholera . . . was reduced almost to nil. . . . And when we say cholera we mean by it a severe attack of virulent true epidemic Asiatic cholera." The statistical evidence is of mortality in the same cholera ward before treatment was begun, which was 4 deaths out of 16 cases bacteriologically proved (25 per cent.), compared with 4 deaths out of 140 bacteriologically proved (2.8 per cent.) after the cases were

taken over for treatment. The patients treated had fully developed cholera symptoms, and were already in a collapsed condition or fell into collapse within six hours of admission. Treatment consisted in the use of intravenous salt solution and the administration of bacteriophage.

The strength of the hypertonic salt solution was 120 grains of sodium chloride to the pint of distilled water and of the isotonic solution 60 grains to the pint. Sterilization of these solutions, after filtration, was done under pressure in the autoclave (30 mins. at 120° C.) and not by boiling, as the boiling drives off dissolved air and renders the solution less efficacious for intravenous injection. An alkaline solution is prepared by the addition, just before use, of a powder of 160 grains of sterilized sodium bicarbonate to 1 pint of sterile isotonic salt solution. It is essential always to take the specific gravity of the blood before intravenous administration. If this is " below 1058 the patient usually does not yet require an intravenous saline." Administration of 1/250 grain of strophanthin is very beneficial. The salt solution should be administered slowly and a rate of an ounce a minute should rarely be exceeded. At a first sitting in adults it was usual to give 3 pints of the hypertonic salt solution and finish off with an additional pint of alkaline salt solution.

The important treatment with bacteriophage is very simple. It is given undiluted in about drachm doses every 30 minutes and two bottles each containing 50 cc. will be finished by direct sipping from the bottle, in the first 16 hours. After the first 24 hours, one bottle in the next 48 hours will generally suffice. Bacteriophage may also be given intravenously in 5 cc. doses for more rapid action, but it must be greatly diluted and is best administered with the salt solution. One word of warning is given regarding the bacteriophage. It should be of the highest virulence possible and have a very wide range of action.

W. F. Harvey.

METZ (M.). Traitement du choléra. [**Treatment of Cholera.**]—*Rev. Méd. de France et des Colonies.* 1930. Aug. Vol. 7. No. 8. pp. 352–359.

The author is the medical officer in charge of the Pnom-Penh hospital, Cambodia, and this paper refers to the results produced by two special methods of treatment: The first of these consists of injections of novarsenobenzol and sulfarsanol in moderate doses. The actual doses given are not recorded but the author maintains that these products sterilize and influence the toxaemia; and notes that 0·06 cc. of sulfarsanol dissolved in 1·0 cc. of water prevents coagulation in 100·0 cc. of normal blood. The second method employed was the transfusion of blood from patients convalescent after cholera, called the serum method. In 1927 forty-six cases of cholera were treated in the Pnom-Penh prison; 27 by what the author calls—without details—the " ancient method," 3 recovered and 24 died; 19 were treated by the " chemical method," and of these 17 recovered, 2 died. From September, 1927, to September, 1928, sixty-four serious cases of cholera were treated in the Pnom-Penh hospital: 17 by the " ancient method " with 2 recoveries; 30 by the " chemical method " with 17 recoveries; 15 by the " serum method " with 7 recoveries and 2 by the " mixed method " with 1 recovery.

J. H. T. W.

DHAR (D. R.). **Action of Kaolin on Vibrio Cholerae and Some Toxins.**—*Calcutta Med. Jl.* 1930. Nov. Vol. 25. No. 5. pp. 207–214. With 3 charts in text. [3 refs.]

In a previous communication it was shown that the adsorption rate by kaolin was much more rapid in the case of *Vibrio cholerae* than with an emulsion of equal strength of coli and typhoid; and quick adsorption is one of the reasons why kaolin in massive doses is beneficial in the treatment of cholera. [This *Bulletin*, Vol. 26, p. 87 (Dhar & Sen).] To find out the nature of cultural characteristics and the behaviour in growths of living cholera, vibrio experiments were carried out. Colonies on agar tubes, containing different proportions of kaolin, were counted; but no clear mathematical data evolved. But it was very definitely established that very heavy proportions of kaolin had a hampering effect on the growth of *V. cholerae.* The chemical nature of kaolin is such that only physical action is possible. The nature of this action is in keeping with the facts noticed with colloid substances.

J. H. T. W.

SEN (Atindra Nath). **Atropine in Cholera.**—*Indian Med. Gaz.* 1931. July. Vol. 66. No. 7. pp. 390–391.

The use of atropine in cholera was suggested by Lauder BRUNTON in 1894 and first tried by Sir Leonard ROGERS, who recommended its use from the earliest stages of the disease. Dr. Sen discusses the action of the drug and the kind of cases in which it is of value.

J. H. T. W.

MINERVIN (S. M.). Ueber Veränderungen des Choleravibrio bei Passage durch den immunen Organismus. [**Changes of the Cholera Vibrio with Passage through an Immunized Animal.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1931. Mar. 18. Vol. 112. No. 2. pp. 242–245. [6 refs.] [Microbiol. Inst., People's Commissariat for Public Health, Moscow.]

Various observations have shown that in persons who have recovered from cholera non-agglutinable vibrios appear in the stools and that during epidemics of cholera the so-called cholera-like vibrios are found in greater numbers than usual. These observations have inspired the the work of the author, who injected true cholera vibrios into the testicles of immunized rabbits. For the most part the inoculations of the testicles, excised 3 to 10 days later, into media were sterile. In two cases, however, one of 4 days' interval, the other of 10 days', colonies were obtained on agar. The organisms obtained from these colonies showed marked differences from the original strains, such as, almost imperceptible growth, slimy colony formation, flocculent suspension, non-motility, morphological change, inagglutinability with cholera serum, want of formation of surface pellicle, loss of virulence, etc. A restoration to the true cholera type was obtained in course of time by subculturing. The changes are interpreted as a transformation of the true cholera vibrio to the cholera-like vibrio.

W. F. Harvey.

YASUDA (Saburoji). [**Immunological Study of Cholera Vibrio killed by Chloroform Vapour.**]—*Sei-i-Kwai Med. Jl.* 1930. July. Vol. 49. No. 7. [In Japanese. English summary p. 7.] [Tokyo Jikeikwai Med. School, Tokyo.]

The comparison made is between cholera vibrios killed by chloroform vapour and by heating for one hour at 60° C. In the case of chloroform-killed vibrios antibodies are more quickly produced and so protection against infection more quickly attained. Heated vibrios are slightly more toxic than chloroform-killed vibrios. The antigenic properties of a suspension when it is kept in an ice chest are retained for at least a month.

W. F. Harvey.

i. SHOUSHA (A. T.). La réaction d'agglutination de groupe dans le choléra. [**Group Reaction of Agglutination in Cholera.**]—*Bull. Office Internat. d' Hyg. Publique.* 1931. June. Vol. 23. No. 6. pp. 1022–1037. [16 refs.]

ii. BUCHANAN (George S.). La bactériologie du vibrion cholérique dans ses rapports avec les questions administratives. [**The Bacteriology of Cholera from an Administrative Point of View.**]—*Ibid.* pp. 1038–1041.

iii. CUMMING (Hugh S.). Rapports entre les vibrions non-agglutinables et les vibrions cholériques. [**Relation of Non-Agglutinable Vibrios to the Cholera Vibrio.**]—*Ibid.* pp. 1042–1045.

iv. GRAHAM (J. D.) [Documents communicated by]. Distribution géographique et répartition par mois du choléra dans l'Inde Britannique de 1919 à 1928. [**Geographical and Seasonal Distribution of Cholera in British India from 1919 to 1928.**]—*Ibid.* p. 1046. With 1 chart & 1 folding map.

i. Two vibrios, Nos. 20 and 67, were isolated at the quarantine laboratory of Tor, one from a normal pilgrim, the other from a pilgrim with dysentery. Each of these strains agglutinated in high degree with the laboratory anti-cholera serum. It was found, however, in the Public Health laboratory of Cairo that No. 20 vibrio was not agglutinated by their anti-cholera serum, while the Tor laboratory serum agglutinated both the standard cholera vibrio of the Public Health laboratory and No. 20 vibrio. This led the author to an elaborate study of the "antigenic structure" of the abnormal Tor strains and to the conclusion that the serum which was being used at Tor contained both "major" or specific agglutinin to the true *Vibrio cholerae* and "minor" or group agglutinins to strains such as vibrios Nos. 20 & 67—in other words, that these latter vibrios were not true cholera vibrios. The importance of this judgment may best be realized from the recommendations of the author in regard to the use of diagnostic cholera agglutinating sera. These are that :—

(1) The ordinary agglutination procedure for the diagnosis of cholera should be coupled with tests in which heated suspensions (containing the specific thermostable antigen) are used ;

(2) a serum should be kept for cholera diagnosis which has been obtained by immunization of an animal with heated suspensions so as to exclude group reaction ;

(3) arrangements should be made for the production of a standard

cholera serum which could be used by all laboratories concerned in the diagnosis of cholera.

ii. In this note there are put forward many of the points on which decisions are required. In the matter of diagnostic agglutination tests it is essential to come to a conclusion what are the differences which can exist between vibrios isolated from different acute cases and in different epidemics. The thermostable antigen is probably the best index of the potential pathogenicity of a suspected vibrio.

The existence of healthy carriers is still a matter of controversy and therefore of great administrative difficulty. Air-travel brings its own special problems to the authorities. Anti-cholera vaccine is of little value for the elimination of carriers and is therefore chiefly useful for the protection of an individual who is rapidly transported to a country in which cholera is rife. Protection of the traveller is, of course, also a means of protection for the general population.

iii. A number of papers are referred to under this heading and the general deduction is that there is little positive proof of the relationship of the two types of vibrio.

iv. These communications consisted (1) of a map of India giving the mean mortality from cholera for its several provinces and districts during the 10 years 1919–1928 and (2) of a very useful diagrammatic figure showing mean cholera mortality month by month in the various provinces during the same period.

W. F. Harvey.

FINKELSTEIN (M. H.). **Problems in the Bacteriology of Cholera and Cholera-like Infections.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1931. June 30. Vol. 25. No. 1. pp. 29–38. [32 refs.] [Bact. Dept., Univ., Edinburgh.]

In this lecture the author deals with some of the outstanding problems of cholera and its causative vibrio. The clinical manifestations which are to be included as true cholera, the relationship of the paracholera and water vibrios to the *Vibrio cholerae*, the variability and serological types of *V. cholerae*, the existence of true carriers in the same sense as for typhoid and the use of bacteriophage in cholera all receive consideration.

W. F. Harvey.

SCHÜTZ (Franz). Ueber den Stickstoffverbrauch der Choleravibrionen zum Aufbau ihrer Leibessubstanz (plastische Quote). [**Nitrogen Requirements (Plastic Quota) of the Cholera Vibrio.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1931. Mar. 18. Vol. 112. No. 2. pp. 287–297. [13 refs.] [Hyg. Inst., Univ., Berlin.]

Nutritive materials may be said to serve two purposes in the life both of higher organisms and lowly bacteria, those connected with the output of energy and those concerned with growth and reproduction. These may be called the dynamogenic quota and the plastic quota of metabolism respectively. It is the utilization of nitrogen for the plastic quota which is here investigated with the following results :—

The media used were fluid and contained 0·03, 0·06 and 0·1 per cent. nitrogen. They also contained 0·5 per cent. glucose. Growth was continued for 1 to 4 days and the cultures then centrifuged. It was found that the centrifuged deposit from 100 cc. of culture furnished

1·99 to 0·25 mgm. nitrogen, which corresponded to a utilization of 4·09 to 0·62 per cent. of the nitrogen of the nutrient medium. No evidence was found that the nitrogen content of the medium exerted any influence upon the quantity of the nitrogen in the deposit. The same negative result was obtained when the nitrogen content for a given number of vibrios was correlated to the nitrogen content of the medium.

W. F. Harvey.

LULL (G. F.). **Cholera and Prophylactic Vaccination in the Philippines.** —*Milit. Surgeon.* 1931. May. Vol. 68. No. 5. pp. 645–648.

The author wisely states that " conclusions as to the protective power of cholera vaccine cannot be drawn without careful controls " but considers that the results of the epidemic studied are worth reporting. His deductions are that at least two doses of cholera vaccine should be given and that vaccination modifies the course of infection.

W. F. Harvey.

RAJU (V. Govinda) & SARKAR (Abhay Kumar). **The Results of Prophylactic Cholera Inoculation in Faridpur District.**—*Indian Med. Gaz.* 1931. Mar. Vol. 66. No. 3. pp. 135–137.

These results have special reference to the use of a single prophylactic dose of cholera vaccine and are based for their estimates of the number of non-inoculated at risk on the recorded population of a district in which a severe epidemic of cholera had broken out. Inoculation was started at the beginning of the epidemic. The case-incidence figures by this mode of computation are 3·3 per mille of 52,295 inoculated and 16 per mille of 203,956 uninoculated. Details are given for individual villages.

W. F. Harvey.

HASSELMANN (C. M.). Bericht ueber gegenwärtige Choleraepidemie auf den Philippinen und die Möglichkeit einer Weiterverbreitung in andere Häfen. [**Cholera in the Philippines and the Possibility of its Spread to Other Ports.**]—*Deut. Med. Woch.* 1931. Jan. 16. Vol. 57. No. 3. pp. 109–111.

The author describes outbreaks of cholera from 1925 to the present time and discusses the possibility of the disease spreading to other ports and lands.

J. H. T. W.

TOMB (J. Walker) & MAITRA (G. C.). **Report on an Investigation on Cholera in the Asansol Mining Settlement, Bengal, India.**—*Jl. Trop. Med. & Hyg.* 1931. Feb. 16. Vol. 34. No. 4. pp. 49–55. [10 refs.]

This paper refers to work done and observations made during the years 1925 to 1928. The material used has already appeared in other publications [this *Bulletin*, Vol. 24, pp. 460–461 and Vol. 27, p. 14].

J. H. T. W.

HEAT STROKE.

CAZAMIAN (Pierre). Coup de chaleur et "crampes" des chauffeurs (étude clinique, pathogénique, prophylaxie, traitement). [**Heat Stroke and Fireman's Cramp.**]—*Arch. Méd. et Pharm. Nav.* 1928. Apr.–May–June. Vol. 118. No. 2. pp. 102–115.

Dr. Cazamian is a naval surgeon and this paper is a careful study of heat stroke as it occurs in steam ships including heat exhaustion and "cramps." He considers the clinical aspect, pathogeny, prevention and treatment of heat stroke generally and points out that "cramps" occur most frequently in the muscles of the extremities, then in the abdomen and quotes the view of Cl. BERNARD and VALLIN that coagulation of myosin takes place in the affected muscles. Many other workers are referred to. In serious forms of cramp he recommends injections of ether, caffeine, oil of camphor and intravenous injections of glucose 47/1,000. Bleeding may be necessary when there is auto-intoxication, morphine, warm baths at 30° C., atropine and similar drugs. The patients should drink plenty of fluid not too cold. [See this *Bulletin*, Vol. 23, p. 457 (*U.S. Nav. Med. Bull*).]

J. H. Tull Walsh.

HAMILTON (C. S. P.), BASU (D. N.) & VAN HAEFTEN (J.). **Review of Cases of "Effects of Heat" (Heat-Stroke, Anidrosis and Heat Exhaustion) occurring during the Hot Weather of 1929 at Allahabad.** —*Jl. Roy. Army Med. Corps.* 1930. Aug. Vol. 55. No. 2. pp. 120–125. With 1 text fig.

The authors describe twenty cases of heat stroke which occurred among the troops in Allahabad in 1929. They were mild cases and no deaths occurred. For sixteen days before the first case, the maximum temperature had ranged from 105° to 113° F., whereas the minimum was never below 84° F. The lowest wet bulb reached 66° F. for one day and averaged 75° F.; whereas the dry bulb reading had never been below 90° F.

J. H. T. W.

SPERO (L. P.). **A Fatal Case of Heat-Stroke.**—*Jl. Roy. Nav. Med. Serv.* 1929. Jan. Vol. 15. No. 1. pp. 53–54.

On September 15, 1928, H.M.S. *Dahlia*, on patrol at the southern end of the Red Sea, received a wireless message from the tug *St. Just*:—"Very urgent; man been unconscious with heat stroke for two hours." An hour and a half later the tug was sighted. The patient, a fireman, aged 54, was lying in his hammock in convulsions. The history given was that a few days previously the man was excused duty as he found his duties in the boiler room very trying. Feeling better he returned to work. He suffered from headache in the forenoon of the 15th and later collapsed, the boiler room temperature being 140° F. Another tug had lost a man from heat stroke a few days previously. The patient was transferred to the *Dahlia* which proceeded to Aden. The man was in convulsions, with periods of coma; rapid, shallow respirations; pupils contracted; temperature 109° F.; pulse 100. Rectal injections of iced water, iced sheets and a rectal injection of chloral hydrate and pot. bromide reduced the temperature to 104° F. and the convulsions ceased. In the night the temperature rose to 107° F. Saline was injected subcutaneously under each breast four times and seemed beneficial for later he showed signs of returning

consciousness and was able to suck pieces of lint soaked in glucose and bicarbonate of soda solution. In the early morning he developed a distinct smell of acetone in his breath, with Cheyne-Stokes breathing ; temperature not above 105° F. At Aden the patient was transferred to the European Hospital. He died a few hours later.

J. H. T. W.

FOY (H. Andrew). **A Note on Recurrent Attacks of Heat-Stroke and Sun Traumatism in the Same Individual.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1930. Nov. 25. Vol. 24. No. 3. pp. 353–354.

The authors describe a case of two major and two minor attacks of heat stroke in the same individual. In such a patient it would appear that some predisposing constitutional condition such as an acid metabolic excess renders him susceptible to the effects of the sun's rays. The man was living in Nigeria and the first major attack occurred at 35 years of age, the second at 46, when the symptoms were more serious. The man came to England in June 1920 and was admitted to the Hospital for Tropical Diseases, London. Recovery was slow, but five months later the patient returned to Nigeria.

J. H. T. W.

TAKEUCHI (Yoshio). Ueber den Blutbefund bei Hitzschlag und Sonnenstich. [**The Blood in Heat Stroke and Sun Stroke.**]—*Jl. Oriental Med.* 1929. Nov. Vol. 11. No. 5. [In Japanese. German summary p. 148.] [Faculty of Imperial Kyushi Univ., Fukuoka, Japan.]

The author has discussed the blood condition in sun stroke and heat stroke as found by other workers. As the outcome of the results of his own experiments he finds that there are considerable changes in the blood both in sun stroke and heat stroke ; they correspond to and follow the rise of temperature and general symptoms. As a rule there is not much loss in erythrocytes or haemoglobin ; but such loss does occur in serious cases. Frequently there is leucopenia. Generally the " pseudoeosinophile " leucocytes and the large monocytes increase while, in contrast, the eosinophile leucocytes and the lymphocytes diminish. After the experiments the blood returns to normal by degrees.

J. H. T. W.

RENNIE (D. C.). **Notes on the Cold (Anti-Heat Stroke) Ward at Masjid-i-Suleiman, South Persia.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1930. Apr. 17. Vol. 23. No. 6. pp. 645–648.

The author describes a special " anti-heat " ward in the Persian Oil Company's hospital, at Masjid-i-Suleiman, built and ready for use in 1927. The refrigerating plant is a single horizontal ammonia compressor working in conjunction with the brine circulating system. The ward and air lock entrance are well insulated. The building is artificially lighted and there are no windows. No case has gone on to heat stroke since the ward was opened ; operations, accidents, burns, etc., have been treated with success and saving of time and the ward has given a sense of security to the staff. Patients are gradually withdrawn from

the ward after recovery. No case of bad effects has occurred from return to the surrounding high temperature. The cost amounts to between £400 and £500 per annum.

J. H. T. W.

MARSH (Frank). **The Etiology of Heat-Stroke and Sun Traumatism.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1930. Nov. 25. Vol. 24. No. 3. pp. 257–276. With 5 figs. [23 refs.]

This paper deals with a series of experiments carried out at Abadan in S. Persia during the summer of 1929, the object being to discover some of the factors involved in the causation of sunstroke and sun traumatism. The shaven heads of a number of albino and black rabbits were exposed to the direct rays of the sun. The bodies of some of the animals were artificially cooled by wetting and a blast of cool air, while the fur of other animals was kept dry and no artificial cooling employed. Almost without exception the animals in which the body temperature was kept from rising by the cooling measures adopted were able to withstand the effects of the sun. On the other hand, the vast majority of the dry, un-cooled rabbits succumbed to heat stroke. The black rabbits were found to be more susceptible to heat stroke than the albinos. The conclusion is drawn that the heat rays, and not the ultra-violet rays of the solar spectrum are responsible for the production of heat stroke which develops when the general body temperature rises to critical heights. It is contended that "sunstroke," "heat-stroke," "heat exhaustion," "insulation" and "sun traumatism" are all conditions of "hyperpyrexia due to heat."

A plan and description is given of the heat-stroke ward in the hospital of the Anglo Persian Oil Company at Masjid-i-Sulieman, and the treatment of patients is briefly dealt with.

An interesting discussion on the paper is given in which the following questions were dealt with: clothing worn in the tropics; the geographical distribution of heat-stroke; sweating; and the increased danger of hyperthermia occasioned by heavy muscular work and fatigue.

G. P. Crowden.

MARTIN (Charles J.). **Thermal Adjustment of Man and Animals to External Conditions.**—*Lancet.* 1930. Sept. 13, 20 & 27. pp. 561–567; 617–620; 673–678. With 17 text figs. [99 refs.] [Summary appears also in *Bulletin of Hygiene.*]

In this series of three Croonian Lectures to the Royal College of Surgeons Sir Charles Martin deals with the mechanism of temperature regulation in man particularly under conditions met with in warm climates. He emphasizes the importance to man of this power of adaption to environment. "By establishing a temperature around 40° C. which, from the materials of which animals are constructed, provides the maximum activity attainable, the homoeothermic animal achieved an immense advantage over its poikilothermic contemporaries." The mechanism for maintaining this relatively constant condition depends for its efficiency on automatic control both of heat production and of heat loss by the body, aided by an intelligent use of "adjustable insulation," which enables man to withstand greater extremes of external temperature than would otherwise be possible. The temperature of the surroundings, the moisture in the air and air movement determine

the heat lost by the body by radiation, convection and evaporation. A comfortably clothed individual sitting in a room at 15° C. and 50 per cent. relative humidity loses 44 per cent. of excess heat by radiation, 31 per cent. by convection and 20 per cent. by evaporation of moisture from lungs and skin, but in hot surroundings evaporation of sweat may be the only mechanism for heat loss. A resting man produces some 1·2 large calories of heat per minute which if lost by evaporation of moisture would mean a loss to the body of at least 2 cc. water per minute (1 gram of water evaporated absorbs 585 small calories). Strenuous work would necessitate the evaporating of approximately a pint of moisture per hour, and there must be a corresponding intake of water by the individual. Sir Charles states that he had great difficulty in impressing these physiological facts on the military authorities during some of the desert campaigning in the summer of 1916.

The nervous mechanism of thermotaxis and the nervous control of the vessels in the skin and of the sweat glands is described. The evidence of the existence of a central co-ordinating mechanism is examined and the development of thermal adjustment is dealt with from the view point of comparative physiology. The source of animal heat and the rate of heat production as influenced by such factors as food and exposure to cold are studied, and Sir Charles recounts some interesting experiments on himself carried out during a voyage through the tropics, which showed that adaptation to hot climates is partly achieved by a lowering of the basal metabolism by some 12 per cent. The part played by the internal secretion of the thyroid and suprarenals in thermal regulation is also discussed.

In the third lecture, temperature regulation in a warm environment is fully dealt with. The experimental evidence points to the fact that central thermal stimulation, by a rise in temperature of the blood supplied to the brain is more effective than local warmth in producing sweating. The naked body exposed to sunshine may absorb 3,420 calories per minute, or three times its resting heat production. This heat is equivalent to the extra heat which a man would produce when walking at a rate of three and a half miles per hour on the flat.

Finally, the author deals with the important question of work at high external temperatures. He describes some experiments on the bicycle ergometer in which he found that the maximum wet bulb temperature which he could endure, without continuous rise in body temperature while working, was 87° F. In a climate with shade temperatures approximating to those of the skin, a man performing hard manual work would need to evaporate from his skin a litre of sweat per hour to maintain his temperature balance. This is impossible unless such clothes as are worn are very thin and wet. Otherwise the evaporation of sweat takes place too far from the body surface, and its cooling effect diminished. The author therefore concludes that the obstacle to work in hot climates for the European is his conventional clothing. A valuable bibliography is given.

G. P. Crowden.

SLEEPING SICKNESS.

CARPENTER (G. D. Hale). **Report on Sleeping Sickness from January to September, 1929.**—*Uganda Protectorate Ann. Med. & San. Rep. for Year ended 31st December, 1929.* Appendix I. pp. 53–57.

LEE (S. W. T.). **Report on Sleeping Sickness from September to December, 1929.**—*Ibid.* pp. 58–59.

As Carpenter went on leave towards the end of 1929, he decided to limit his report to the first nine months of the year, leaving the last quarter to his deputy, Dr. Lee.

After giving an account of his own activities, the staff available and the introduction of new legislation, Carpenter summarizes the present state of affairs in each sleeping sickness area.

Victoria Nyanza—Nile area. No new cases have been reported in this area, except in the old endemic area of Samia County at Mjanji; it therefore seems probable that the outbreak at Kyadondo has been suppressed. Inspections of the Lake area made during the year show that there is a very real risk that infection once introduced into the islands would find an opportunity for spreading. In many places there are small settlements of a few families living where they are surrounded by *G. palpalis*, and where they can only get water by traversing fly-infested roads. These settlements are quite unable to protect themselves by prophylactic clearings and yet are too small to be worth the expenditure of money in paid labour. Recommendations made in the past that such small settlements should not be allowed have not met with the approval of the Administration. The author considers that very close administrative supervision of the conditions under which the people live is essential if sleeping sickness is to be prevented from establishing itself on the islands and mainland coast.

Busitema and Mpologoma areas. These have not been toured; in both sleeping sickness is in abeyance.

Siroko Valley area. The population was examined by Carpenter and no new cases of sleeping sickness were found.

Lake Edward-George area. Only the Kigezi portion of the area was toured; no new cases were found.

Bwamba Valley area. This was not examined.

Wasa River area. Constant trespass into this "restricted area" was found to be taking place by natives hunting illegally.

Buganda-Lake Albert area. In the absence of medical supervision it has not been possible to proceed with the establishment of the fishing village at the south end of Lake Albert as arranged last year.

Bunyoro area. Carpenter visited the Murchison Falls and made recommendations as to clearing necessary to safeguard visitors to the falls.

Gulu area. (*a*) *Acholi.* The recommendations made by Dr. FREETH had been carried out and the situation was immensely improved. The whole population of the fly-infested area was examined and only 2 new cases found among 26,535 persons examined. During 1928, Dr. FREETH had discovered 116 new cases, but up to August of 1929, only 27 new cases had been reported.

(*b*) *Madi.* Capt. FREEMAN before he left Madi examined the population and reported in East Madi 11 new cases among 3,106 persons examined and in West Madi 6 new cases out of 10,400 examined. There seems to be evidence that sleeping sickness may again be increasing in Madi.

Chua area. There has been no medical officer at Kitgum during the year. In November, 1928, sixteen cases had been reported at Paranga. Carpenter, who visited the place in April, 1929, found that very extensive clearings had been carried out ; 3 new cases and 2 suspects were found among 1,519 persons examined.

West Nile area. The report in this area is disquieting ; the epidemic continues to spread. The total number of cases found between the middle of 1928 and September, 1929, is : Aringa 1,167, Junam 539, Madi Ai-avu and Midiri 96, Omugo 38, Kobokko 8, Arua township 7, Terego 1. A disquieting fact is the case found at Terego, a county from which no cases have hitherto been reported ; others will probably be found.

Carpenter's report closes with some remarks on recruitment of labour.

ii. Lee carried out a tour of the Eastern Province sleeping sickness area during November and December. The outbreak in the West Nile area showed signs of abating. In the Gulu area there was an increase in the number of deaths in the Madi district ; this increase is significant in view of the fact that for the greater part of the year no medical officer was available for duty in either Madi or Gulu.

Nine cases of sleeping sickness were treated at Kitgum in the Chua area in 1928, but during 1929 the number rose to 39 proved cases and 20 suspects.

The remaining areas in Uganda have produced no increase in the number of sleeping sickness cases. Clearings are reported to have been adequately maintained and the position appears to be satisfactory.

W. Yorke.

PRATTI. Note sur la palpation et ponction des ganglions cervicaux dans la pratique itinerante. [**Palpation and Puncture of Cervical Glands in Itinerant Practice.**]—*Ann. Soc. Belge de Méd. Trop.* 1931. Mar. 31. Vol. 11. No. 1. pp. 75–90.

The author lays particular stress on the fact that his observations in this paper apply to work in the field and not to hospital or laboratory work. The engorged cervical glands, which serve as a guide in the diagnosis of trypanosomiasis vary in site, size, form, consistency and number.

Position. The enlarged glands may be unilateral or bilateral ; there may be isolated enlarged glands or groups of glands. Similarly, sometimes the superior glands are involved and at other times the inferior glands. The author draws attention to many other conditions than trypanosomiasis which may give rise to enlarged cervical glands and points out that one of these may co-exist with trypanosomiasis.

Size. A gland, which in the normal state is not palpable, may in trypanosomiasis enlarge to the size of a pigeon's egg. The author distinguishes the following gradations. i. Pin-head. ii. Small. iii. Moderately small. iv. Moderate. v. Large.

Whilst the superficial glands are easy to palpate, the deep glands are more difficult and require experience. The fact that glands escape notice on palpation and are difficult to puncture is not due to their small size, but to the fact that they are deeply placed beneath the muscles.

A good palpation involves three procedures : (*a*) Deep palpation. (*b*) Superficial palpation. (*c*) Palpation à plat in which the palmar

surface of the hand is passed over the surface of the neck ; enlarged glands, which otherwise may escape notice, are detected by the radial side of the index finger.

Form. This is generally ovoid, but sometimes round and sometimes elongated. The contours are always regular and rounded, and the glands are not adherent to the skin or tissues, so that they roll easily under the fingers.

Consistency. The typical glands are of the consistency of a ripe plum. Although, however, this is characteristic of trypanosomiasis, it must not be forgotten that there are other affections which may give rise to the same phenomenon. If, on the one side, this condition is not exclusive to sleeping sickness, there are glands of other kinds which are positive on puncture.

During the evolution of the disease the glands hypertrophy and then, having reached their maximum, they progressively diminish in size and in elasticity and lose their characteristic appearance. On palpation of a chain of glands it is possible sometimes to appreciate quite easily glands in different stages of evolution and involution. In patients in the sleeping sickness stage glands are often to be found which exhibit a remarkable degree of sclerosis and, however, may be positive on puncture.

The author then passes to an analysis of his own observations. He contrasts the results of puncturing groups of a 100 each of individuals with large glands, moderate glands, small glands, and very small glands : 95 per cent. of the first were positive, 12 per cent. of the second, 4 per cent. of the third, and 1 per cent. of the fourth. From this he concludes that the value of gland formulae is directly proportioned to their size. It is remarked that enlarged glands are, of course, more likely to be due to sleeping sickness in heavily contaminated regions than in regions where the disease is merely sporadic. He illustrates this by observations in two localities. In the first, where the number of infected was about 12 per cent., 6,195 persons were examined. Of those with large glands, 84 per cent. were positive ; with moderate glands 40 per cent. ; with small glands 18 per cent. ; and with very small glands 11 per cent. In the second district, where the intensity of infection was only 2 per cent., 2,797 patients were examined. Of those with large glands 84 per cent. were positive ; with moderate glands 11 per cent. ; with small glands 4 per cent. and with very small glands 1 per cent. From these figures it is apparent that the large glands have the same value in each district, but the smaller glands have less significance in the sporadic region than in the epidemic region.

Further work showed that the value of the examination of the lymphatic glands is greater in adults than in children, and that this applied equally to glands of large and small size.

W. Y.

HAMERTON (A. E.). **Remarks on Trypanosomiasis in Relation to Man and Beast in Africa.**—*Jl. Roy. Army Med. Corps.* 1931. Mar. Vol. 56. No. 3. pp. 161–166. [6 refs.]

Although he has modified the opinions concerning the desirability of exterminating wild animals in " fly " country, which he held in 1913, when a member of the Royal Society's Commission on Sleeping Sickness,

the author considers that " the alleged rôle of the great African Fauna in maintaining the tsetse fly population and the incidence of human trypanosomiasis or sleeping sickness is still a debatable point." In the present article he has attempted to state very briefly the case for and against the game, and incidentally to mention some of the more important observations which have caused him to modify his former views.

There appears to be little doubt that the large ungulata have been almost exterminated in certain parts of the country and the tsetse has remained in these districts as elsewhere. Various examples are referred to in support of this statement. Hamerton writes " No man can foretell the result of depriving the tsetse of its accustomed diet of wild animals' blood " [It was for precisely this reason that many years ago the reviewer and others advocated the carrying out of a scientific experiment] ; but so long as there are men and cattle about the " fly " will not starve. Evidence is accumulating in support of the view that game destruction instead of being a remedy increases the danger from the fly by causing dispersal of the insects which subsequently concentrate around villages in the bush where they feed mainly on man and inoculate into his blood certain animal-derived parasites which in the game are harmless, but become lethal when introduced into man and his domestic animals. [This may be true, but before he could accept it as a fact the reviewer would require very convincing evidence that *G. morsitans* could flourish unperturbed when its main food supply had disappeared. If so it is indeed an animal greatly to be envied. Again, if it be a fact that when in an area the game is destroyed the fly tends to concentrate round the villages in that area in order to attack man, why not devote attention to reasonable clearings round those villages ? Finally, whence, in the absence of game, would the tsetse draw the " animal-derived parasite " to inoculate into man ?]

After referring to evidence indicating that a trypanosome normally and harmlessly living in the blood of game animals may, under certain conditions, become adapted to living in human blood in which it develops lethal properties, Hamerton passes to a consideration of the converse process where trypanosomes pathogenic to man may after prolonged sojourn in game become non-pathogenic to man. In support of this hypothesis reference is made to the present state of affairs in the Sese Islands, to the experimental inoculation of man with game trypanosomes by Taute and Huber, and to the recent experimental investigations by the reviewer and his colleagues. [This short paper is worth consulting in the original by those interested in this important subject.]

W. Y.

Kleine (F. K.). Erfahrungen einer ärztlichen Studienreise nach Ostafrika. [**Medical Experiences in a Visit to East Africa.**]—*Deut. Med. Woch.* 1931. Jan. 23. Vol. 57. No. 4. pp. 153–155. [2 refs.] [Robert Koch Inst., Berlin.]

The author spent two years in Tanganyika Territory, and continued as far as he was able his work on the trypanosome infections. At the mission at Sikonge, near Tabora, he inoculated 24 sheep with the blood of 24 sleeping sickness patients. There remained alive, after 2 months 17, after 3 months 10, after 4 months 6, after 9 months 3 ; two

apparently made a complete recovery. Three of the strains were subinoculated from sheep to guineapigs, the blood of which was examined every fifth day till their death and 500 trypanosomes counted. In one guineapig, which survived 75 days, posterior nuclear forms were never seen. Though it is conceivable that infected sheep might be a source of danger to man, all epidemiological studies point to man to man infection. Possibly the virulence of the trypanosome in wild or domestic animals steadily gets less ; it would be a simple experiment to find out.

Turning to chemotherapy he comments on the part played by the animal host. Germanin is effective in *T. rhodesiense* infection in man, but is useless in the same infection of cattle. On the other hand, antimosan is very effective in cattle but has no action in trypanosomiasis of man. He notes the variability of the trypanosome content of the cerebrospinal fluid and quotes the case of a child previously treated with tryparsamide in whose C.S.F. there were on one occasion 750 parasites per cmm. and a week later only a single trypanosome was detected, though no fresh treatment had been given. Of various remedies which he tried none was comparable with germanin.

A. G. B.

SCHILLING (Claus). **Spontaneous and Experimental Infection.**—*Jl. Trop. Med. & Hyg.* 1930. Nov. 15. Vol. 23. No. 22. pp. 334–336. [Robert Koch Inst., Berlin.]

The author points out that among the great number of enigmata confronting the epidemiologist and parasitologist, one of the most interesting is the puzzle of the healthy carrier. Why is invasion not equivalent to infection ? Why does a child carrying toxin-forming diphtheria bacilli in his throat not necessarily suffer from diphtheria ? Why does a carrier of the poliomyelitis virus not develop poliomyelitis ?

After referring to a number of recent observations on yellow fever and malaria bearing on this subject, the author passes to trypanosomiasis. Many observers have shown that " genuine " strains isolated from naturally infected animals have a low virulence for mice and rats, whilst old laboratory strains killed these animals within a few days. Moreover, the antigenic qualities of genuine and old laboratory strains are different. BRAUN and TEICHMANN and Claus Schilling have tried in vain to immunize with genuine trypanosomes ; this can only be done with old laboratory strains. Again, the sensitiveness to the action of chemotherapeutic drugs undergoes modifications as the result of a long series of transmissions from animal to animal without interpolating the insect host.

In 1912–1924 the author and the late Hans SCHRECK carried out a number of experiments on the tsetse-free island of Makatumbe near Dar-es-Salaam. They had at disposal a strain of *T. brucei* kept at Hamburg in small animals for many years (Strain Hamburg alt), and *G. morsitans* bred from pupae and therefore free from infection. The flies were fed on a rat infected with Hamburg alt, then on normal cows, likewise infected, and afterwards on a normal rat. With the new strain " Hamburg recens," passed through the fly, the following experiments were executed :—

Calf, about 3 weeks old, infected February 27th, 1914, with Hamburg recens. On March 5th and 16th very scanty trypanosomes in the blood. (Sera always heated at 45° C. for 30 minutes to kill the trypanosomes of the donor.)

(*a*) Serum of the day of infection, February 27th, 1914.

Mouse.		Days after							
		1	2	4	5	6	9	13	18
1.	Serum alone ...	0	0	0	—	0	0	0	0 experiment closed
2.	Serum + Hamburg alt ...	+	++	+++	dead				
3.	Hamburg alt alone ...	+	—	+++	dead				
4.	Serum + Hamburg recens ...	0	0	0	++	+++	+++	+++	dead
5.	Hamburg recens alone ...	0	0	+	+++	+++	+++	+++	dead

Trypanosomes *in vitro* : after 30 minutes trypanosomes in all tubes motile.

(*b*) Serum of the 36th day after infection.

Mouse.		Days after							
		1	2	3	4	5	14	23	30
1.	Serum + Hamburg alt ...	0	+	++	dead				
2.	Hamburg alt alone ...	0	0	++	+++	dead			
3.	Serum + Hamburg recens ...	0	0	0	0	0	0	0	0 experiment closed
4.	Hamburg recens alone ...	0	0	++	+++	+++	+++	dead	

Trypanosomes *in vitro* after 30 minutes contact with serum :
Hamburg recens nearly all motionless.
Hamburg alt actively motile.

Other experiments with the same strains showed the same phenomenon of specific action. They were compared with a genuine strain from a gnu killed in the bush. Virulence and sensitiveness to serum of the gnu strain were the same as the Hamburg recens.

Schilling claims from this work to have shown : (*a*) an old laboratory strain of *Trypanosoma brucei* is far different in virulence and antigenic qualities from a genuine strain ; (*b*) such a laboratory strain is changed in its most important qualities by one passage through the natural transmitter, i.e., the glossina ; (*c*) it is restored to the qualities of a genuine strain.

[This is an important piece of work and requires confirmation. It does not seem to be in harmony with Duke's statement that arsenic resistance is transmitted through glossina. There is some evidence to be found in the literature that it is not easy to pass old laboratory strains through glossina, but Schilling apparently experienced no special difficulty.]

W. Y.

DUKE (H. Lyndhurst). *Trypanosoma gambiense* **in Monkeys and Ruminants ; Prolonged Infection, Immunity and Superinfection.**—*Parasitology.* 1931. July. Vol. 23. No. 3. pp. 325–345. [7 refs.] [Human Trypanosomiasis Inst., Entebbe.]

The author commences by stating again certain conclusions reached in two previous papers (this *Bulletin*, Vol. 25, p. 764, and Vol. 26, p. 205). The object of the present paper is to submit further evidence on two important points—firstly, the ability of ruminants, domestic and otherwise, to serve as reservoirs of *T. gambiense*; and secondly, the effect on this species of trypanosome of prolonged sojourn in a single mammalian host. In this paper there is presented all the evidence on these two subjects now available in the Entebbe records, old and new, published and unpublished. These must be consulted in the paper by those interested.

Duke states that his experiments show a remarkable agreement in testifying to a decrease in the transmissibility of *T. gambiense* when it remains for long in one and the same animal. The infectivity of the strain to the gut of tsetse, apart from its transmissibility, also tends to diminish as the sojourn in the mammal increases. The diminution in the adaptation of a strain to tsetse may progress to complete loss of transmissibility, and when once this stage is reached it is highly improbable that transmissibility can ever be recovered. There is good reason to believe that in many cases the diminution is the effect of inhibitory influences exerted on the trypanosomes in the course of time by the tissues of its mammalian host, and that the strain once freed from these influences by introduction into another and non-immune host may recover in this new host, temporarily at all events, its original transmissibility.

The transmissibility of a strain, although greatly reduced, may persist for a long time, often up to the death of the host ; thus trypanosomes in 4 sheep were still infective to fly 12 to 18 months after their original infection. We do not know whether these strains after their long stay in an individual mammal are still capable of infecting man. It is, therefore, quite clear that *T. gambiense* can persist in a transmissible form in sheep for more than a year and, indeed, until the death of the animal from some intercurrent disease or accident, for there is no evidence that infection with strains of *T. gambiense* recently isolated from man necessarily shortens the life of sheep and goats. Some sheep and goats show complete resistance to infection with *T. gambiense ;* and some of the 19 strains of *T. gambiense* were much less able to survive in a transmissible form in sheep and goats than were others.

It is very probable that in addition to individual differences between different strains in their ability to utilize tsetse, individual mammalian hosts differ in their attitude towards the trypanosome, some being more congenial to it than others.

In nature revival of the transmissibility of a strain by the agency of inoculation into a new host must be an exceedingly rare event. Direct transmission is essentially dependent on the presence of numerous trypanosomes in the peripheral blood, and in the chronic infections under consideration this condition is probably never fulfilled. There is little evidence that cyclical passage through fly has the same stimulating effect on the strain as direct inoculation into a new host.

These experiments suggest that from the epidemiological point of

view the chief danger is the recently infected vertebrate host in which the trypanosome is best able to exercise to the full its powers of utilizing tsetse. Chronic cases are much less dangerous owing to the inhibition of the transmissibility of the trypanosome by prolonged contact with the tissues of one and the same host. Experience of the last few years generally confirms Conclusion 4 of the International Commission's Report, viz., that the transmissibility of *T. gambiense* is greater in the human patient than animals infected from him, whether infection be by fly-bite or by the syringe.

In three strains of polymorphic trypanosomes from natural sources other than man, transmissibility by tsetse has been lost during a period of maintenance by syringe passage of many months' duration. Other strains isolated from man have been found to be non-transmissible in subinoculated animals ; and one strain obtained in a monkey inoculated from a situtunga was found to be completely non-transmissible and all but non-infective to tsetse. All this work suggests very strongly that the depression of transmissibility not uncommonly proceeds to the point where this property is permanently lost. The existence, so commonly reported by observers of sleeping sickness, of sporadic cases of human trypanosomiasis in fly-infested native populations, where the disease shows no signs of spreading, is thus easily explained, since in such cases the trypanosome cannot pass cyclically through tsetse.

Superinfection. For several reasons superinfection is important to the present discussion. First, it is an accident that must frequently befall both men and animals exposed to tsetse in nature ; and secondly, by means of the transmissibility test, superinfection renders possible the recognition of a degree of immunity not appreciable by any test previously devised. An account is given of three sheep, a goat, and four monkeys, which were subjected to superinfection. In the case of one monkey successive infections led to successive revivals of the transmissibility of the strain. In the second monkey, which had been infected only 4½ months, superinfection produced no discernible change. A third monkey, superinfected with a transmissible strain after six months, failed to become infected. The fourth was superinfected two months after the original infection and for the first time became infective to the glands of fly. The first sheep superinfected with a homologous strain of *T. gambiense* 15 months after the first infection, and at a time when the original strain was still transmissible, failed completely to infect the glands of fly. A second sheep superinfected after 16 months' contact with *T. gambiense* failed to respond in any way, and four months later superinfection with a heterologous strain of *T. gambiense* likewise completely failed. The third sheep was infected originally with a feebly transmissible strain which never infected fly. Superinfection 17 months later with a heterologous strain of *T. gambiense* failed to produce any change ; but a second superinfection, after a further 2½ months, with *T. rhodesiense* was immediately established and rapidly killed the animal. The goat was treated in a manner similar to the third sheep and behaved in much the same way.

It would appear that prolonged infection with *T. gambiense* leads to the development in the mammal of an immunity against this trypanosome. This immunity acts first upon the transmissibility of the strain by tsetse and has no demonstrable effect on the mere presence of trypanosomes in the animal's circulation. The transmissibility is reduced to a low level and is sometimes abolished altogether. There is reason

to believe that whereas this immunity gradually develops in the course of an infection with a single strain, superinfection stimulates its production and intensifies its effect.

W. Y.

BLANCHARD (M.) & TOULLEC (F.). Un cas de trypanosomiase africaine à évolution lente. [**Case of Trypanosomiasis of Slow Development.**]—*Marseille-Méd.* 1931. Jan. 25. Vol. 68. No. 3. pp. 110–112. [1 ref.]

The authors quote from the literature to show that the length of the first stage (blood lymphatic) may vary very greatly before the disease passes into its second stage and the meninges are invaded. They record in considerable detail a case in which it is possible to fix exactly the date when the patient left the endemic region. He was admitted to hospital at Marseilles on March 19th, 1929, as a case of tuberculous adenitis. The history shows that he had been recruited at Ouagadougou and had left Dakar on February 15th, 1927. During the two years he had served in France without any illness until March, 1929, when in the course of a tuberculosis inspection he was diagnosed as a case of this disease and sent to hospital.

On examination nothing abnormal was found, except general enlargement of the lymphatic glands—cervical, axillary, inguinal, and mediastinal. As their consistency suggested trypanosomiasis one of them was punctured and trypanosomes found. Lumbar puncture gave lymphocytes 2, albumen 0·1, no trypanosomes.

W. Y.

BARLOVATZ (A.). L'exploration méningée dans la maladie du sommeil. [**Meningeal Exploration in Sleeping Sickness.**]—*Bull. Soc. Path. Exot.* 1930. Dec. 10. Vol. 23. No. 10. pp. 1014–1020.

The object of this paper is in the first place to add to the data which have already appeared and in the second place to recommend in lumbar and suboccipital punctures the use of a fine needle as less of a shock to the patient.

The importance of examination of the meningeal fluid in the control of sleeping sickness is recognized by all, but it is still not generally used in routine diagnosis. The author's figures favour its general use and he is convinced that of all the methods it is the most useful.

A single examination of blood, no matter how made, allows of the escape of a very great number of cases, and the same can be said of gland puncture, especially as all patients have not got puncturable glands. At the Pandji hospital during the first five months of 1930, 49 cases were recognized by gland puncture as against 63 in whom lumbar puncture suggested very strongly a diagnosis of trypanosomiasis. One can safely assert that 20 per cent. of the infected in an endemic region do not exhibit parasites in the glands at the time of examination and that at least half do not show them in the blood.

After discussing the results obtained by lumbar puncture the author concludes that although it has not the scientific and diagnostic value of the demonstration of trypanosomes in the blood or gland juice, yet it furnishes signs—increased cell count and so forth—of the first value which afford strong presumptive evidence of sleeping sickness. Alterations in the spinal fluid—great or slight—exist, at least in Mayumbe, in 85 to 90 per cent. of the infected cases taken at random. In a similar group of patients a single search for the parasite in the

blood or gland juice does not enable a diagnosis to be made in more than 70 per cent. of cases.

It appears, then, legitimate to examine the cerebrospinal fluid of all natives coming from a heavily infected region. The author has never had occasion to travel in such a district, but he makes a suboccipital puncture in every native, coming from an endemic area with more than 1 or 2 per cent. of new cases per year, who complains of indefinite symptoms of unknown causation. Often enough he finds alterations in the spinal fluid and sometimes profound changes (1,500 cells) without any definite reason to suspect such.

If meningeal exploration is to be generalized it must of course be harmless and as little painful as possible. Of the 5,000 punctures made in the author's service since 1926, none has been fatal: nevertheless, even a needle of 0·6 mm. bore often causes severe headache. Since the beginning of the present year the author has abandoned lumbar puncture for suboccipital puncture. He uses needles 0·6 mm. in diameter and 5 cm. in length. As such fine needles pierce the native skin with difficulty, he makes an incision first. Over 2,000 suboccipital punctures have been made with only two accidents—aseptic meningitis, as the result of considerable haemorrhage, which recovered in a week or two. In both these, needles of 0·9 mm. diameter were used and two punctures were made as the fluid did not flow from the first. The author notes that the suboccipital region is very vascular and the introduction of the needle into the muscular tissue of the neck often leads to a considerable haemorrhage.

W. Y.

BARLOWATZ. Le liquide céphalo-rachidien chez quelques trypanosés devenus arsénorésistants pendant le traitement. [**The Cerebrospinal Fluid in Trypanosomiasis Patients who became Arsenic-resistant during Treatment.**]—*Ann. Soc. Belge de Méd. Trop.* 1930. Dec. 31. Vol. 10. No. 4. pp. 415–421.

The author draws attention to a peculiarity of the cerebrospinal fluid met with in certain arsenic-resistant cases of trypanosomiasis which he has had to deal with at Mayumbe. He has previously published a series of secondary arsenic-resistant cases [this *Bulletin*, Vol. 26, p. 708, and Vol. 27, p. 816 and 829] and he now records others.

These are patients who have been treated either with atoxyl or tryparsamide, or more frequently with both drugs, for several years, apparently with success; suddenly there was a relapse and the trypanosomes were found no longer to yield to tryparsamide or other arsenicals. In general the patients were examined as to the state of their lymphatic glands every six months, and in certain of them lumbar puncture was performed at the same time. The results are summarized as follows:—

Cerebrospinal fluid with 2·6 to 4 leucocytes	5
Cerebrospinal fluid with normal leucocytes	17
Cerebrospinal fluid with more than 4 leucocytes ...	10

The quantity of albumen present agreed with the leucocyte count. These results are compared with those obtained from 158 cases punctured immediately on diagnosis; amongst these only 16·5 per cent. had less than 2¾ leucocytes per cmm.

Secondary arsenic-resistance appears then in a certain number of patients as a new invasion of the organism, which runs a similar course to the original infection. The trypanosomes appear to hide themselves not in the central nervous system, but in one or other of the tissues and to become little by little resistant to tryparsamide. This differentiates clearly secondary arsenic-resistance from a single failure of arsenical treatment in which one finds—especially with atoxyl—a changed cerebrospinal fluid with a peripheral circulation which is often sterile. Brief notes are given concerning 21 of the cases upon which the author has based his argument.

RODHAIN, in the discussion which followed the paper, refers to Barlowatz's hypothesis that during and after the first treatment the parasites have sought shelter in tissues other than the nervous system, and adds that other possibilities occur to him, notably that the patients were reinfected. RODHAIN does not believe that gland puncture is a good method of diagnosing relapses; he considers that it is blood examination that will give information regarding arsenic resistance.

W. Y.

i. PERGHER (Joseph). Technique nouvelle pour l'étude de la cytologie du liquide céphalo-rachidien. [**New Technique for the Study of the Cytology of the Cerebrospinal Fluid.**]—*Ann. Soc. Belge de Méd. Trop.* 1930. Dec. 31. Vol. 10. No. 4. pp. 381–383. [Bact. Lab., Leopoldville.]

ii. VAN DEN BRANDEN (F.), DUMONT (P.) & NÉLIS (P.). Etude critique sur la valeur d'une nouvelle méthode de dosage de l'albumine du liquide céphalo-rachidien. [**A New Method of estimating the Albumen of the C.S.F. Critical Study.**]—*Ibid.* pp. 405–414. [3 refs.] [Central Lab., Administration of Hyg., Brussels.]

i. Cytological study of the cells in the cerebrospinal fluid is unsatisfactory owing to the difficulty of spreading preparations and in getting them to adhere to the slide. The author has devised the following method which, thanks to its simplicity, can be used in the bush :—

In 5 cc. of a 1·5 per cent. solution of sodium citrate in distilled water 0·4 gm. of gelatine are dissolved by the aid of heat : the reaction, which is acid, is adjusted so as to be slightly alkaline. The solution is filtered through filter paper. One or two drops of this gelatine solution is added to 1 cc. of a 1 or 2 per cent. solution of sodium citrate in a centrifuge tube heated to 37–38° C. Lumbar puncture is then made and a few cubic centimetres of the fluid allowed to fall directly into the centrifuge tube, which is then centrifuged at low speed for 10 to 20 minutes, and the supernatant fluid removed. A small drop of the gelatine solution is placed on a slide and by its side a drop of the deposit from the centrifuge tube ; the two drops are then mixed together and spread. The author attaches much importance to the actual making of the films. The quicker the films dry the better the preservation of the cells ; hence, as little fluid as possible should be used in a relatively strong concentration of gelatine. The best results are given by fluids rich in albumen, and when the cerebrospinal fluid contains but little albumen a small quantity is added to the gelatine.

The gelatine assures the adhesion of the cells to the slide and assists in their staining.

ii. In this article the authors compare the value of Arnaud's new method of estimating the albumen in cerebrospinal fluid [this *Bulletin*, Vol. 27, p. 237 and p. 853] with the classical method of Sicard and Cantaloube. The observations they have so far made do not indicate that Arnaud's method should supercede Sicard and Cantaloube's: the former method does not result in complete precipitation of the proteins, and consequently the figures resulting are less than those obtained from the classical technique.

W. Y.

SICÉ (A.), BOISSEAU (R.), PROVOST (J.) & DENIEL. Le quotient albumineux du sérum chez quelques trypanosomés. [**The Serum Proteins in Trypanosomiasis.**]—*Bull. Soc. Path. Exot.* 1931. Mar. 11. Vol. 24. No. 3. pp. 181–184. [1 ref.] [Pasteur Inst., Brazzaville.]

The authors have studied the chief proteins in the serum of a number of cases of sleeping sickness in various stages of the disease. Blood was taken from 13 natives at the same time in the morning; all were on the usual diet of cassava and dried fish. The amount of albumen was determined according to the technique of Hammarsten by saturation of the serum with magnesium sulphate. Of the 13 natives two, who served as controls, were perfectly healthy subjects. The serum of the first gave a protein total of 80·5 per cent.; the serum albumen was 49·3 and the globulin 31·2 (ratio 1·58): the second gave a protein total of 77·8 per cent. with albumen 47·2 and globulin 30·6 (ratio 1·54).

The remaining 11 cases all suffered from trypanosomiasis (*T. gambiense*); 3 were in the first stage and 8 in the meningeal stage. Details of the estimation of the serum proteins in these cases are given in a table. The infected cases may show a considerable diminution in total serum proteins and the loss is mainly due to a decrease of serum albumen. The ratio $\frac{\text{serum albumen}}{\text{globulin}}$ is always less than it is in normal persons.

W. Y.

CORSON (J. F.). **Observations on the Cerebrospinal Fluid in Nine Cases of Rhodesian Sleeping Sickness during Treatment with Bayer 205 and Tryparsamide.**—*Ann. Trop. Med. & Parasit.* 1931. Aug. 13. Vol. 25. No. 2. pp. 189–193. [2 refs.]

The observations recorded in this paper were made at Maswa in Tanganyika Territory. It was thought that possibly somewhat frequent examinations of the cerebrospinal fluid, made during periods of from about 6 to 12 months, in patients continuously under treatment with Bayer 205 and tryparsamide, might yield data which could be a guide to prognosis and treatment.

Details of the treatment and results of repeated spinal punctures in nine cases are given in a table. The cell count did not fall to normal in any of the patients, but in four of them there was a considerable reduction lasting some months. In one case a relapse, with fever and

trypanosomes in the blood, occurred about the eighth month, although there had been a reduced cell-count for several months before. In another case a total of 50 gm. of tryparsamide within a period of seven months had no apparent effect on the cerebrospinal fluid.

It is remarked that in these cases the dose of Bayer 205 was almost invariably 1 gm. ; that of tryparsamide ranged from 2 to 4 gm., usually 2 or 3 gm., given at weekly intervals.

The following are the conclusions :—

" The significance of a reduction of the cell-count of the cerebrospinal fluid to a normal figure cannot be judged from these cases. No inferences as to prognosis in general and treatment can be drawn from the observations. It would seem that the prognosis in all these cases is unfavourable, and that treatment should be continued for want of something better and to guard others.

" The observations indicate that neither Bayer 205 nor tryparsamide can be regarded as likely to cure advanced cases of Rhodesian sleeping sickness, and this is in accordance with clinical experience."

W. Y.

CORSON (J. F.). **A Further Note on Some Cases of Rhodesian Sleeping Sickness treated at Ikoma, Tanganyika Territory, in 1926 and 1927, including Those under the Care of Professor F. K. Kleine.**—*Ann. Trop. Med. & Parasit.* 1931. Mar. 31. Vol. 25. No. 1. pp. 63–68. [3 refs.]

In September, 1930, the author visited Ikoma and made enquiries about cases of sleeping sickness treated by KLEINE and himself in 1926 and 1927. Details of 39 of these were published in a previous paper [this *Bulletin* Vol. 26, p. 697]. The first 37 of these had been under KLEINE's care ; a further 27 cases were treated by Corson up to October 9th, 1927.

The results of treatment of the 64 cases are shown in a table. Twenty-nine (45·3 per cent.) were reported to be alive and eighteen were seen. All were said to be well except two. KLEINE's cases did not do so well as the author's, 12 only being reported alive out of 37, whilst 17 of Corson's 27 were living. The difference is said to be due to the later batch containing a greater proportion of early cases, owing to the fact that by the middle of 1927, the people got to know the doctors and to recognize the quick beneficial results of treatment. The summary is as follows :—

" 1. Of sixty-four patients who received thorough treatment, twenty-nine were reported to be alive about three or more years later. Twenty-seven, or 42 per cent., may be regarded as recovered. This high figure is due to the number of early cases that came for treatment, especially during the later months of the year 1927.

" 2. There is no indication, from a study of these cases, that any trypanocidal drug, except Bayer 205, can cure Rhodesian sleeping sickness.

" 3. When a parasitic blood relapse has occurred, the prognosis is very unfavourable. In all except a few cases, no form of treatment or combination of trypanocidal drugs seems to lead to cure. Nervous symptoms are sometimes relieved by Tryparsamide when Bayer 205 has failed and the converse occurs, but the relief is only temporary.

" 4. One case, viz., No. 46, appears to be one of recovery of a patient with an infected central nervous system."

W. Y.

NAJERA (L.). La punción de la cisterna cerebelo-medular y su importancia en la tripanosomiasis humana. [**Puncture of the Cerebello-Medullary Space and its Importance in Human Trypanosomiasis.**]—*Medicina Países Cálidos.* Madrid. 1930. Nov. Vol. 3. No. 6. pp. 520–526. With 3 text figs. French summary (8 lines).

The author states that suboccipital puncture through the occipito-atloid ligament into the cisterna cerebello-medullaris is a simple procedure, devoid of all risk, more easily carried out than lumbar puncture, and of service in cerebral oedema, hydrocephalus, and uraemia, but particularly in sleeping sickness, either for withdrawing fluid or introducing drugs. He has performed the operation on about

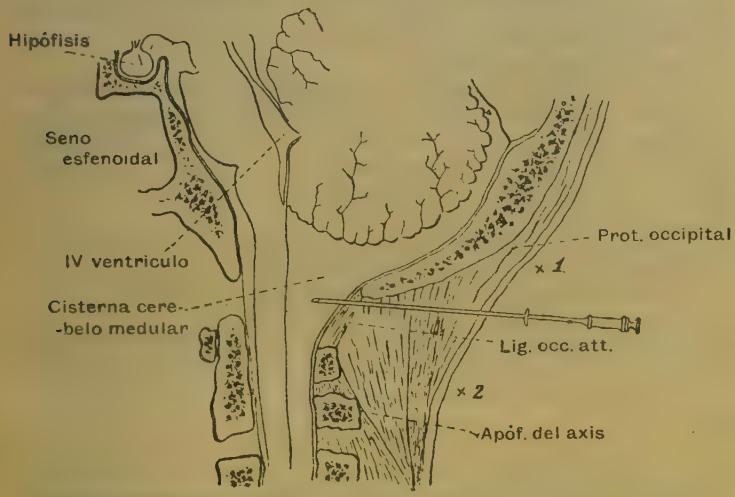

Diagram illustrating position of trocar in making suboccipital puncture through occipito-atloid ligament into the cisterna cerebello-medullaris.

[Reproduced from *Medicina de los Países Cálidos.*]

400 patients without the slightest mishap and states that many present themselves voluntarily at the hospital to have it done, as they prefer it to lumbar puncture. A diagram shows the technique, which appears to be very simple.

H. H. S.

SICÉ (A.). L'Institut Pasteur de Brazzaville et la trypanosomiase humaine. [**The Brazzaville Pasteur Institute and Human Trypanosomiasis.**]—*Bull. Soc. Path. Exot.* 1931. Jan. 14. Vol. 24. No. 1. pp. 5–14.

In this address Sicé summarizes the sleeping sickness work of the Pasteur Institute at Brazzaville. The Institute is responsible for Brazzaville and surrounding country.

The disease among the European population of the Congo is slight, only 0·56 per cent. being infected. If, however, the officials, who formerly were heavily infected and are now almost free, are excluded, the remainder of the European population—traders, missionaries, etc.—are infected to the extent of 1·47 per cent.

Among the native population the results are much more encouraging. In 1910, of a total of 4,330 examined at the Pasteur Institute 324 (7·4 per cent.) were infected ; in 1929, of 23,510 persons examined only 228 (0·9 per cent.) were infected. No less than 87·5 per cent. of the infected have come up spontaneously for examination—gland puncture and spinal puncture.

Passing to the subject of chemotherapy the author states that the arsenobenzols and acetylarsan have given very inconstant results. He leaves Bayer 205 and Fourneau 309 to a future communication, and limits himself in the present paper to a discussion of the results obtained with atoxyl, either alone or associated with emetic, Fourneau 270, tryparsamide and tryponarsyl.

Atoxyl. Between 1906 and 1919 almost all the 2,797 patients treated at Brazzaville received atoxyl and in almost every case the injections were less than 1 gm. The results were not striking. From 1920 to 1928, the patients, 1,118 in number, were given doses of 15 to 20 mgm. per kilo of body weight. Of these, 663 have been followed carefully ; they can be divided into three groups :—

316 with only blood and lymphatic infection,
208 with lesions of the cerebrospinal system,
139 unclassified as spinal puncture was not performed.

Of the 1st group, 249 are cured—198 without any other drug and 51 with the ultimate use of tryparsamide ; 43 are dead and 24 have disappeared. Of the 2nd group, 34 are cured—2 without any other drug and 32 with the aid of tryparsamide ; 1 has improved, 141 are dead and 32 have disappeared. Of the 3rd group, 62 are cured—45 without other drugs and 17 with the aid of tryparsamide ; 63 are dead and 14 have disappeared. It is remarked that during this work it was found that 105 (15·9 per cent.) exhibited blood relapses and that of these 11·1 per cent. occurred during the first year of treatment.

Tryparsamide. Here are grouped together cases entirely treated with this drug and those previously treated unsuccessfully with other drugs. Of 51 cases in the first stage of the disease 19·6 per cent. have had blood relapses and 3·9 per cent. have progressed and presented meningeal lesions. Of 256 patients with nervous involvement 4·6 per cent. have had blood relapses, 16 per cent. have again relapsed with nervous symptoms, and 8·9 per cent. have died. The results given with tryponarsyl, the Belgian product, have been identical.

Fourneau 270. This is the sodium salt of acetyl-p-amino-o-oxyphenyl arsenic acid. Between 1925 and 1929, 357 cases have been treated. Of the 106 patients in the first stage of the disease 3·7 per cent. have had relapses, 2·8 per cent. have progressed to the nervous stage and 33 per cent. have not been followed up. Of 251 patients in the second stage of the disease, 3·5 per cent. have had blood relapses, 13·1 per cent. have progressed, 51·3 per cent. have had prolonged amelioration sometimes definite, 14·3 per cent. have died and 17·5 per cent. have disappeared.

The doses of tryparsamide and Fourneau 270 varied from 15 mgm. to 35 mgm. per kilo ; the injections were given every seven days.

The author contrasts the results obtained with these three drugs in the following tables :—

Patients in the first stage of the disease.

	Atoxyl.	Tryparsamide.	"Fourneau 270."
	Per cent.	Per cent.	Per cent.
Blood relapses ...	15·9	19·6	3·7
Nervous developments	25·0	3·9	2·8

Patients in the second stage of the disease.

	Atoxyl.	Tryparsamide.	"Fourneau 270."
	Per cent.	Per cent.	Per cent.
Blood relapses	—	4·6	3·5
Progressive evolution ...	—	16·0	13·1
Dead	67·0	8·9	14·3

The accidents following the use of tryparsamide were practically nil. Some precautions were necessary in the case of Fourneau 270. It may produce vomiting some hours after administration, and in advanced cases may be followed by visual troubles going on to blindness.

It is stated that of the five compounds prepared by Dr. STRATMAN THOMAS of Wisconsin, viz., 73-etharsanol, 115, 130, 134 and 139, only 115 gave results approximating to those of tryparsamide.

W. Y.

VAUCEL (M.) & BOISSEAU (R.). L'action du moranyl dans l'arséno-résistance de la trypanosomiase humaine. [**Action of Moranyl in the Arsenic Resistance of Human Trypanosomiasis.**]—*Bull. Soc. Path. Exot.* 1931. May 13. Vol. 24. No. 5. pp. 374–378. [5 refs.] [Pasteur Inst., Brazzaville.]

This work, which was undertaken at Brazzaville, relates to the action of moranyl (Bayer 205) in cases of human trypanosomiasis resistant to arsenicals ; most of the patients were in the meningeal stage and had been unsuccessfully treated with tryparsamide.

A. Meningeal cases. As the cases were all very similar the results are not given separately in detail, but are summarized in a table. The injection of tryparsamide invariably resulted in an amelioration of the condition and in a return of the condition of the cerebrospinal fluid towards the normal. The author considers arsenic-resistance to be indicated by a stabilization of the cerebrospinal formula and a persistence of the albumen at about 0·40 ; this condition presages invariably a renewal of the evolution of the disease. Such cases are relatively rare. More frequently after an apparent clinical cure with normal cerebrospinal findings there is found, after a lapse of 3 to 6 months, an increase of albumen in the spinal fluid. A further course of tryparsamide may again produce a normal spinal fluid, but generally

speaking the excess of albumen indicates the development of a relapse on which arsenic has no action.

When once arsenic-resistance, whether initial or after a relapse following an adequate course of treatment, has developed, it is useless to continue arsenical treatment.

As the table shows, a check is almost all one can hope for from the treatment of such cases by moranyl. In only a single case did the cerebrospinal fluid become normal. The author points out that he does not hesitate to classify as " checks " all cases in which the albumen of the spinal fluid fails to fall below 0·35 no matter whether the cell count has become normal or not ; such cases always relapse.

B. Gland and blood cases. It is unfortunately true that prolonged treatment with tryparsamide, notwithstanding the magnificent effects on the cerebrospinal fluid, is frequently followed by the reappearance of trypanosomes in the blood. Relapses are still more frequent after shorter courses given to patients in the first stage of the disease. At the Pasteur Institute of Brazzaville tryparsamide is no longer used for the treatment of early cases. It is replaced by Fourneau 270 [acetyl-p-amino-oxyphenyl arsenic acid] which gives only 3 per cent. of relapses as compared with 18 per cent. for tryparsamide. Even cases in which tryparsamide fails are susceptible to Fourneau 270 and likewise to atoxyl. If, however, it is a case of true arsenic-resistance moranyl is indicated. An illustration is quoted at length.

The author considers that amongst the many trypanocidal substances available for use in the first stage of the disease tryparsamide is the worst. He uses Fourneau 270 with confidence, or in cases of intolerance (especially vomiting in women) the combination atoxyl-emetic. When there is true arsenic resistance he advises moranyl alone or with emetic. In the second stage of the disease tryparsamide alone can be employed with any hope of success.

W. Y.

LAUNOY (L.) & PRIEUR (Marie). Actions trypanocides synergiques du 205 Bayer–309 Fourneau et d'un sérum spécifique, dans la trypanosomiase expérimentale à *Trypanosoma Brucei*, de la souris. [**Synergic Action of Bayer 205 and Specific Serum in Treatment of Experimental Trypanosomiasis in Mice.**]—*Bull. Soc. Path. Exot.* 1931. Apr. 15. Vol. 24. No. 4. pp. 311–327. [1 ref.]

Cats which have been protected against *T. brucei* by a prophylactic injection of Bayer 205 [this *Bulletin*, Vol. 27, p. 834] develop, when the refractory state is past, infections, the evolutions of which are very inconstant. As a rule these infections are very prolonged and may sometimes terminate in spontaneous cure. Usually the normal virulence of the parasite is recovered at the second passage, but this is not invariably the case. Details are given of series of mice infected from two of the authors' cats in which the infections ran prolonged courses for several passages through mice and only gradually recovered their normal virulence.

The authors believe that this diminution in the virulence of the virus is due to two antagonistic factors, viz., specific antibody and minute traces of drug. A large number of experiments is recorded which show that a fraction of the curative dose of Bayer 205, i.e., $\frac{1}{4}$ suffices, when given with the specific serum obtained from nagana-infected rabbits, to cure mice infected with *T. brucei*.

W. Y.

DUBOIS (A.). A propos de l'action " in vitro " de la tryparsamide sur les trypanosomes. [**Action of Tryparsamide on Trypanosomes in Vitro.**]—*Ann. Soc. Belge de Méd. Trop.* 1931. Mar. 31. Vol. 11. No. 1. pp. 93–99. [6 refs.] [School of Trop. Med., Brussels.]

The author refers to the work of the reviewer and his colleagues on the trypanocidal action of arsenicals *in vitro* [*ante*, p. 350]. He is particularly concerned with the statement that pentavalent arsenicals, such as tryparsamide, are but slightly trypanocidal *in vitro*, viz., 1 : 200 in 6 hours and 1 : 1,600 in 24 hours at 37° C. As BRUYNOGHE and Dubois had found that tryparsamide was inactive *in vitro* at laboratory temperatures, the author determined to re-examine the subject, using the reviewer's technique and conducting his observations at 37° C. He worked with *T. pecaudi* and his results were similar to those of the reviewer.

Dubois enquires whether the results could be explained on the hypothesis that the serum of the nutrient medium converted the tryparsamide into trypanotoxyl, but came to the conclusion that this was not the explanation.

W. Y.

KOLMER (John A.) with the Assistance of Anna M. RULE. **The Prophylaxis of Experimental Trypanosomiasis by the Oral Administration of Arsenical Compounds and Germanin.**—*Amer. Jl. Trop. Med.* 1931. July. Vol. 11. No. 4. pp. 261–272. [6 refs.] [Research Inst. of Cutaneous Med., Philadelphia.]

The author has conducted experiments on rats with a view to ascertaining whether the oral administration of such drugs as stovarsol, treparsol, atoxyl, tryparsamide, and Bayer 205 had any prophylactic action against infection with *T. equiperdum*.

His conclusions are as follows :—

" 1. Stovarsol and treparsol in doses of approximately 0·030 to 0·040 gram per kilogram of weight by oral administration for three to ten days were effective in preventing trypanosomiasis of rats infected with *Tr. equiperdum*.

" 2. Atoxyl was slightly more effective, as doses of 0·020 to 0·030 gram per kilogram per day by oral administration for five to ten days prevented infection.

" 3. Tryparsamide by oral administration was ineffective in dose of 0·050 gram per kilogram once a day for five to ten days.

" 4. ' Bayer 205 ' or ' Germanin ' was ineffective in dose of 0·020 gram per kilogram of weight by oral administration once a day for three to ten days.

" 5. As a general rule these compounds were slightly more effective when their administration was started twenty-four hours after infection than when given before infection.

" 6. If *Tr. gambiense* and *Tr. rhodesiense* are as susceptible as *Tr. equiperdum* to stovarsol, treparsol and atoxyl, it would appear that the oral administration of these compounds in amounts without danger of producing toxic amblyopia or other toxic manifestations, like 4 tablets a day for a week at a time followed by an intermission, may be of practical value in the prophylaxis of trypanosomiasis of human beings temporarily exposed to infection."

W. Y.

LOURIE (E. M.). **The Effect of 'Höchst 4002' on** *Trypanosoma gambiense* **and** *T. evansi* **in Mice and Rats.**—*Ann. Trop. Med. & Parasit.* 1931. Mar. 31. Vol. 25. No. 1. pp. 123–127. [2 refs.]

In view of the promising results obtained by GIEMSA [this *Bulletin*, Vol. 27, p. 832] in the treatment of mice infected with *T. brucei* (Prowazek), the author decided to examine the trypanocidal action of "Höchst 4002" in mice and rats infected with *T. gambiense* and with *T. evansi*.

The conclusions are :—

"The values obtained in the writer's series of therapeutic experiments with 'Höchst 4002' are all very considerably less favourable than those quoted by Giemsa; and it is interesting, in this conclusion, to note that disappointing results have also been recorded by Nieschulz and Wawo-Roentoe (1930), not only in experiments on mice, rats and guineapigs infected with a strain of *T. evansi*, but also in the case of similarly infected horses.

"The prophylactic value of 'Höchst 4002' as judged by the writer's experiments, is negligible."

W. Y.

LÉPINE (Pierre). Action trypanocide du stibiothiopropanol sulfonate de sodium. [**Trypanocidal Action of Stibiothiopropanol Sulphonate of Sodium.**]—*C.R. Soc. Biol.* 1931. June 12. Vol. 107. No. 19. pp. 594–595. [Pasteur Inst., Paris.]

This preparation was made by LUMIÈRE and has the formula :—

$$\begin{pmatrix} CH_2S \\ CH\text{–}OH \\ CH_2SO_3Na \end{pmatrix} Sb_3$$

It contains 15 per cent. of antimony and is a white crystalline substance which slowly turns yellow if exposed to light. Mice tolerate 4 mgm. per 20 gm. of body weight and rabbits 20 mgm. per kilo. It is immaterial whether the drug is given intravenously or intramuscularly.

It has no action on *Sp. duttoni* or *Sp. gallinarum*, but is active in maximum doses on *Sp. pallida* and *Sp. cuniculi*, although relapses soon occur. On rabbits and mice infected with *T. gambiense*, *T. brucei* or *T. evansi* it is definitely active and compares favourably with other antimonials.

W. Y.

LEVADITI (C.), BARDET (J.), TCHAKIRIAN (A.) & VAISMAN (A.). Le gallium, propriétés thérapeutiques dans la syphilis et les trypanosomiases expérimentales. [**Therapeutic Properties of Gallium in Syphilis and Trypanosomiasis.**]—*C.R. Acad. Sci.* 1931. May 4. Vol. 192. No. 18. pp. 1142–1143.

During the course of their studies on the therapeutic properties of certain elements, the authors have discovered that the rare metal gallium is both trypanocidal and spirillicidal. Of the derivatives studied, the tartrate was the most active. It apparently cured experimental syphilis in the rabbit, but failed with the other spirochaetal infections. The curative dose for mice infected with *Trypanosoma evansi* was 4·5 mgm. per 20 gm. of mouse and the tolerated dose 15 mgm. Trypanosomes disappeared from the blood in 24 to 30 hours; some

mice were definitely cured, others relapsed. Similar results were obtained with other trypanosomal infections, viz., *T. brucei*, *T. congolense*, *T. pecaudi* and *T. gambiense*.

W. Y.

YORKE (Warrington), MURGATROYD (Frederick) & HAWKING (Frank). **Studies in Chemotherapy. IV.—The Action *in vivo* of Certain Arsenical and Antimonial Compounds and of Bayer 205 on *T. rhodesiense* and on Atoxyl- and Acriflavine-Resistant Strains of this Parasite.**—*Ann. Trop. Med. & Parasit.* 1931. Aug. 13. Vol. 25. No. 2. pp. 313–349. [4 refs.]

In the 2nd paper of this series the two senior authors recorded the action *in vitro* of certain arsenical and antimonial compounds on *T. rhodesiense* and on atoxyl- and acriflavine-resistant strains of this parasite [*ante*, p. 350]. Now the authors examine *in vivo* the validity of their deductions. The animal was the mouse and injection intraperitoneal. The limitations of this method are detailed, such as the limit to the concentration of drug employable, the lack of information as to the concentration of the drug in the blood. Certain terms are defined :—

" *Minimum Effective Dose* (M.E.D.). The minimum dose which sufficed to clear the blood of at least 80 per cent. of the treated mice, irrespective of time.

" *Minimum Curative Dose* (M.C.D.). The minimum dose which sufficed to cure (thirty days' observation) at least 80 per cent. of the treated mice.

" *Lethal Dose* (L.D.). The minimum dose which killed at least 50 per cent. of the treated mice within twenty-four hours in the case of the inorganic, trivalent organic, and arsenobenzol compounds, and within three to four days in the case of the pentavalent organic compounds."

It is noted that " lethal dose " is used in a special sense and the question of time is discussed at some length, in regard specially to the slow-acting pentavalent compounds.

The result of this work is summed up in 22 tables (occupying 24 pages) in which the following drugs were respectively employed—atoxyl, reduced atoxyl thioglycollate, sodium 4-hydroxy-phenyl-arsonate, 4-hydroxy-phenyl-arsenoxide, arsacetin, reduced arsacetin, tryparsamide, reduced tryparsamide thioglycollate, sodium stovarsol, reduced stovarsol thioglycollate, halarsol, halarsol thioglycollate, novarsenobillon, disodium 4-glycine-phenyl-arsonate, arsenophenylglycine, sodium arsinite, stibenyl, stibosan, tartar emetic, acriflavine, Bayer 205 ; three strains of parasite being employed in each case. The last table gives the lethal doses of the various compounds, the M.E.D. and M.C.D. for the normal and resistant strains and their minimum trypanocidal concentrations for the same strains *in vitro*. The summary of this paper, which must be consulted in the original by serious students, is as follows :—

" 1. An attempt has been made to confirm by experiments *in vivo* the conclusions reached in a previous paper from observations *in vitro* regarding the action of a considerable number of arsenical and antimonial compounds on *T. rhodesiense* and on atoxyl- and acriflavine-resistant varieties of this parasite.

" 2. The minimum effective dose (M.E.D.) and the minimum curative dose (M.C.D.) were determined for each drug in respect of infections in mice produced by the normal strain.

" 3. No differences could be detected between the reactions of the

two resistant strains to the various drugs. Owing to the fact that with most of the drugs these infections resisted doses up to and including the lethal dose, it proved impossible except in the case of disodium-4-glycine-phenyl-arsonate, arsenophenylglycine, stibosan, tartar emetic and Bayer 205, to determine exactly even the minimum effective dose for these strains; and only in the case of Bayer 205 could the minimum curative dose be ascertained.

"4. Notwithstanding the limitations which this fact has necessarily imposed on these *in vivo* experiments, we have been enabled to obtain sufficient information to confirm the main conclusions reached from our *in vitro* work. To the various arsenoxides and arsenobenzols, the resistant strains exhibited different degrees of resistance. For example, in the case of arsenophenylglycine, the M.E.D. for the resistant infections was practically the same as that for the normal infection, whereas in the case of reduced tryparsamide thioglycollate the M.E.D. for the resistant strains was undoubtedly considerably more than sixty times that for the normal strain.

"5. This fact, together with the observation that the resistant infections were no more resistant to sodium arsinite than was the normal strain, indicates that the resistance of the atoxyl- and acriflavine-resistant strains is not a resistance to arsenic but is dependent on the structure of the substituted phenyl radical in the various aromatic compounds of arsenic and antimony.

"6. This contention is supported by the fact that whilst the resistant strains proved to be definitely resistant both to stibenyl and to stibosan, they were just as susceptible to tartar emetic as was the normal strain.

"7. It is interesting to note that the resistant strains responded to Bayer 205 in almost exactly the same manner as did the normal strain.

"8. The facts that the M.E.D. and M.C.D. of the arsenoxides and of the arsenobenzols are exceedingly small as compared with the M.E.D. and M.C.D. of the corresponding pentavalent compounds, and the sterilization of the peripheral circulation is produced more rapidly by the arsenoxides and arsenobenzols than by the pentavalent compounds, support the hypothesis that therapeutic activity in the case of the former compounds is due to the direct trypanocidal effect of the unchanged drugs and in the case of the latter to an indirect action dependent on their reduction, in the body of the host, to the corresponding trivalent forms.

"9. Further strong support to this hypothesis is provided by the observation that both in the case of the normal strain and in that of the resistant strains, there was found to be a close parallelism between the minimum effective doses of the various drugs *in vivo* and their minimum trypanocidal concentrations *in vitro*. In fact, all strains responded in the *in vivo* experiments in precisely the manner in which the previous *in vitro* experiments had indicated that they would respond, on the assumption that the therapeutic activity of the arsenoxides, arsenobenzols, sodium arsinite and tartar emetic depended on the direct trypanocidal power of the unaltered drugs, whilst that of the pentavalent compounds depended on their reduction in the body of the host into their corresponding trivalent forms."

A. G. B.

YORKE (Warrington), MURGATROYD (Frederick) & HAWKING (Frank). **Studies in Chemotherapy. V.—Preliminary Contribution on the Nature of Drug Resistance.**—*Ann. Trop. Med. & Parasit.* 1931. Aug. 13. Vol. 25. No. 2. pp. 351–358. [8 refs.]

The first observation of resistance of trypanosomes to drugs was made in EHRLICH'S laboratory by FRANKE and ROEHL (1907), who fed nagana-infected mice with parafuchsin, to which the parasites developed

a resistance communicable to other mice. A large amount of work has followed. According to EHRLICH this resistance is due to a reduction of the avidity of the specific chemoreceptors for the drug to which the strain has been made resistant. DALE criticized this hypothesis in 1923 and VOEGTLIN, DYER and MILLER (1924) write of "the total inadequacy of this theory" [see this BULLETIN, Vol. 22, p. 142]. Regarding arsenic resistance as a relative term relating the resistance of one strain to that of another strain the authors give two possible explanations: "The strain with the higher resistance may owe its greater resistance either to reduction in permeability of the parasites for the drug, or to a fortification of the natural physicochemical defence mechanism of the protoplasm against the toxic action of the drug."

In support of the second possibility they cite experiments of VOEGTLIN, DYER and LEONARD on the toxic action of arsenoxide with reference to sulphydryl compounds of protoplasm.

"According to Voegtlin's hypothesis—if we understand it correctly—a strain of trypanosomes exhibiting a pronounced degree of drug resistance should, on exposure to a given concentration of the arsenical to which it is resistant, be capable, in virtue of its excess of sulphydryl compounds, of absorbing more of the arsenical than is the homologous normal strain; whilst according to Ehrlich's theory, which postulates that resistance on the part of a strain is due to a reduction of the avidity of its specific chemoreceptors, the resistant strain should be capable of absorbing less of the arsenical, to which it is resistant, than is the normal strain."

Experiments to test this were performed by the author. They cannot be described here. They show that:

"When normal and atoxyl-resistant strains of trypanosomes are incubated at 37° C. for one hour, in nutrient media, containing similar concentrations of reduced tryparsamide, their behaviour is essentially different, in that whilst the normal strain rapidly absorbs the drug, the atoxyl- (or acriflavine-) resistant strain fails to remove any appreciable quantity of the drug from the medium.

"This fact is in harmony with Ehrlich's theory that drug-resistance is due to a lowered avidity of the specific chemoreceptors of the parasite, and also with any hypothesis which explains drug-resistance on the basis of an increased impermeability of the parasite for the drug. It appears to render untenable the hypothesis of Voegtlin, Dyer and Miller, which postulates that a trypanosome strain owes its arsenic resistance to a sufficient excess (above the physiological requirement) of sulphydryl compounds available for combination with arsenic."

A. G. B.

ROSKIN (Gr.). Arzneimittel und ultraviolette Strahlen. VIII. Mitteilung. Zur Methodik der kombinierten Therapie. [**Drugs and Ultraviolet Rays. Method of Combined Treatment.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1930. Vol. 69. No. 3/4. pp. 240–243. [2 refs.] [Microbiol. Research Inst., Education Commissariat R.S.F.S.R., Moscow.]

In earlier published work Roskin and his collaborators have shown that novarsolan plus U.V. rays will sterilize trypanosome-infected mice while novarsolan by itself in the same dose fails. The technique of the experiments is here given. GIEMSA and ELLENBOGEN failed to get the same results and Roskin now points out that these authors did not remove the hair before applying the rays. To ensure their penetration it is necessary to remove all the hair from the mouse's back.

A. G. B.

ROSKIN (Gr.). Arzneimittel und ultraviolette Strahlen. IX. Mitteilung. Beiträge zur Analyse der Kombinierten Therapie. [**Drugs and Ultraviolet Rays. IX. Communication. Analysis of the Combined Therapy.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1931. Vol. 69. No. 5/6. pp. 473–483. [10 refs.] [Microbiol. Research Inst., Education Commissariat R.S.F.S.R. Moscow.]

The author commences by summarizing the previous work of himself and others on this subject [this *Bulletin*, Vol. 27, p. 233 and p. 837]. In the present communication details are given of a number of experiments devised with the object of throwing light on the mechanism of the phenomenon.

The conclusions are :—

1. In the serum of mice which have been subject to ultra-violet radiation there is a special Factor A. This is responsible for the definite increase of the therapeutic action of neosalvarsan on combined treatment of mice infected with *T. equiperdum*.

2. This factor is destroyed by heating at 56° C. for half an hour, and also by ultraviolet radiation of the serum *in vitro*. It is absorbed out of the serum by kaolin.

3. Observations show that the active mesenchyme of the skin and the whole reticulo-endothelial system have a part in the production of Factor A. The serum of splenectomized mice is either entirely lacking in Factor A or contains it in insufficient amount.

W. Y.

GIEMSA (G.) & JÍROVEC (O.). Salvarsan und ultraviolette Strahlen. [**Salvarsan and Ultraviolet Radiation.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1931. Vol. 70. No. 5/6. pp. 466–471. With 1 text fig. [4 refs.] [Inst. for Ship. & Trop. Diseases, Hamburg.]

The authors have re-examined the claim of ROSKIN and ROMANOWA that the action of salvarsan is enhanced by ultra-violet radiation [this *Bulletin*, Vol. 27, p. 233]. Their experiments completely failed to confirm the observations of the Russian workers.

W. Y.

CITRON (Heinrich). Versuche ueber die Beeinflussung der Salvarsanfestigkeit. [**Experiments on the Influencing of Salvarsan-Resistance.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1931. Vol. 69. No. 5/6. pp. 464–472. [42 refs.] [Reich Health Office, Berlin-Dahlem.]

Reference is made to the work of KABELÍK* on the therapeutic properties of sodium thiosulphate, in which the statement is made that this substance is able to overcome drug-resistance. The author mentions that optochin resistance in cases of Ulcus serpens corneae is influenced in a favourable manner by simultaneous administration of thiosulphate. Again, there are the records of WERNIGK, and those of BEINHAUER and JACOB that patients with salvarsan resistant syphilis and a persistent Wassermann reaction can be benefited by the combination of the specific drug and sodium thiosulphate [see *Bull. of Hyg.*, Vol. 3, p. 876].

* *Ztschr. f. Immunitätsforsch.* Vol. 58. p. 434.

Citron has examined the question in an experimental study of mice infected with a salvarsan-resistant strain of *T. brucei*. The resistance of the strain was practically complete in that whilst 1/125 gm. of salvarsan per 20 gm. of mouse cured the infection, smaller doses of 1/250 gm. failed to do so. Four mice were infected with this strain and when parasites appeared in their blood the first was given intravenously an injection of 1 cc. of a 2·5 per cent. solution of sodium thiosulphate and the other three, which served as controls, were given salvarsan in doses of 1/125 gm., 1/250 gm. and 1/500 gm. per 20 gm. of mouse respectively. The sodium thiosulphate had not the slightest influence on the course of the infection, and as soon as parasites were numerous in the blood of the animal which had received this substance, four more mice were inoculated from it. When parasites appeared in their blood one was given sodium thiosulphate and the remaining three controls salvarsan as before. From the sodium thiosulphate animal the strain was carried on as shown in a table until the 22nd passage. The table shows that for the first 17 passages the salvarsan resistant character of the strain remained unchanged, but at the 18th passage it had completely disappeared, so that such minute doses as 1/8000 gm. of neosalvarsan sufficed to cure. A second experiment gave exactly similar results.

W. Y.

ADAMS (A. R. D.). **The Action of Various Sera, *in vitro*, on the Gut and Salivary Gland Forms of *T. rhodesiense* and *T. gambiense* from *Glossina palpalis*.**—*Ann. Trop. Med. & Parasit.* 1931. Aug. 13. Vol. 25. No. 2. pp. 299–311. [4 refs.] [Human Trypanosomiasis Inst., Entebbe, Uganda.]

During the course of an investigation into the action, *in vitro*, of various sera on a number of strains of *T. rhodesiense* and *T. gambiense* in laboratory animals, the opportunity was taken of determining the reactions to these sera of the various stages of the parasites occurring in experimentally infected *Glossina palpalis*.

The following strains of trypanosomes were used in this work :—

" (I) Four strains of *T. rhodesiense* . . . very recently recovered from human cases in the Kahama area of Tanganyika. The majority of the flies used were infected either from the original guineapigs inoculated from man or from monkeys subinoculated from these guineapigs.

" (II) A strain of *T. gambiense* . . . isolated from man in the West Nile area of Uganda early in 1929, and since maintained in a sheep and several monkeys by cyclical transmission through *G. palpalis*."

A detailed account is given of the technique employed, and the results of the experiments are summarized in tables. The original paper should be consulted by those interested.

The following summary is given :—

" 1. A technique is described whereby the action of various sera on the gut and salivary gland forms of the pathogenic trypanosomes from *G. palpalis* can be studied *in vitro*.

" 2. It is shown that these forms, in a suitable medium, can be maintained alive *in vitro* for a period of at least twenty-four hours at laboratory temperatures (24° C. to 29° C.). They usually survive in spite of the considerable bacterial invasion often unavoidably present, and in fairly sterile media generally show definite evidence of multiplication.

"3. The fresh sera of a number of different mammals, birds, and reptiles are rapidly trypanocidal to the gut forms of *T. rhodesiense* and *T. gambiense* recovered from laboratory infected *G. palpalis*.

"4. Heating these sera to 56° C. for twenty minutes, filtering them through a Berkefeld filter candle, or treating them with ammonia destroys their trypanocidal powers. As haemolytic complement is removed by these procedures, but was found to be present in the trypanocidally active sera, it is concluded that complement is the trypanocidal body.

"5. These same sera, even when undeactivated, exert no lytic action on the salivary gland forms of *T. rhodesiense* and *T. gambiense in vitro*. The gland forms are thus shown to differ fundamentally from the gut forms; were this not the case, it would be difficult to account for the infection of mammals by the injection of salivary gland forms.

"6. It has been shown that blood, recovered from recently fed *G. palpalis*, is devoid of haemolytic complement, no complement being detected in blood obtained from flies within ten minutes of feeding.

"7. The presence of an anti-complementary substance has been demonstrated in saline emulsions of the mid-intestines, and to a less extent in those of the salivary glands, of unfed *G. palpalis*, and it is probably due to the presence of this substance that infected flies are not sterilised by subsequent feeds of normal complement-containing blood."

W. Y.

i. CORSON (J. F.). **The Effects of the Injection of Human Blood Serum into White Rats infected with** *Trypanosoma rhodesiense*.—*Kenya & East African Med. Jl.* 1931. Jan. Vol. 7. No. 10. pp. 292–296. [2 refs.]

ii. ——. **Further Observations on the Trypanocidal Action of Human Blood Serum on** *Trypanosoma rhodesiense* **in White Rats.**—*Jl. Trop. Med. & Hyg.* 1931. Mar. 16. Vol. 34. No. 6. pp. 81–83. [5 refs.]

i. On account of the recent work by the reviewer and his colleagues on the action of human serum on trypanosomes [this *Bulletin*, Vol. 27, p. 804], the author records a number of observations which he has made in Tanganyika. The trypanosomes were obtained from natives infected in the Mwanza province. In 6 of the 10 experiments the rats were infected directly from the patients, whilst in the other 4 the rats were infected from sheep or goats in which animals the strain had been maintained by direct passage for about three months.

The serum used came from 8 healthy natives who had never had sleeping sickness, and from an Englishman who had been naturally infected with Rhodesian sleeping sickness in May, 1928. In every instance the serum was given subcutaneously.

Details of the 10 experiments are given and should be consulted in the original by those interested.

The following is the summary :—

"1. In ten experiments in which seven strains of *T. rhodesiense* were used and blood serum from nine healthy persons, there was a great reduction within 24 hours in the number of trypanosomes in the peripheral blood of white rats. Experiment 6 is possibly an exception as on the day of injection the number of trypanosomes was too few to show any striking change.

"2. The effect of the injection of human serum was greater in four experiments in which the trypanosomes had been maintained in sheep

and goats for three months than in the other experiments in which the rats had been infected directly from human beings. In only two of the latter experiments, however, were two cubic centimetres of serum injected.

"3. Although most of the trypanosomes were caused to disappear from the peripheral blood, in no case did a cure result.

"4. It is interesting to recall that Duke (1912) found that the injection of normal human blood serum into monkeys infected with *T. gambiense* caused a temporary disappearance of the trypanosomes from the blood. As this did not occur in the case of rats the author attributed the effect to some condition present in the monkeys which causes them to react to human serum."

ii. This paper, an extension of the previous one, records the results obtained in 36 similar experiments. The results are set forth clearly in a couple of tables which should be consulted by those interested. The author writes :—

"The serum of some persons had more effect than that of others, but that of sleeping sickness patients did not show, on the whole, less trypanocidal action than that of healthy persons."

W. Y.

AMAKO (T. H.). Beiträge zur Kenntnis der Schutzkraft der Milz und des Retikuloendothelialsystems gegen eine Infektion des Organismus durch die *Spirochaeta Duttoni* und *Trypanosoma Gambiense*. [**Protective Power of the Spleen and Reticulo-Endothelial System against Infection of the Organism by** *Sp. duttoni* **and** *T. gambiense*.]—*Fukuoka-Ikwadaigaku-Zasshi* (*Fukuoka Acta Med.*). 1930. Feb. Vol. 23. No. 2. [In Japanese. German summary pp. 12–13.]

——. Ueber die Rolle der Leber und der Milz bei der Antikörperbildung bei experimenteller Trypanosomiasis. [**The Röle of the Liver and Spleen in Antibody Formation in Experimental Trypanosomiasis.**]—*Ibid.* [In Japanese. German summary p. 13.] [Bact. Inst., Imperial Kyushu Univ., Fukuoka, Japan.]

i. In infections of mice and guineapigs with spirochaetes and trypanosomes, the resistance of the animal is most diminished after combined splenectomy and blockade of the reticulo-endothelial system, less so after splenectomy alone, and least after blockade alone. After splenectomy compensation sets in on the fourth day. Leaving a portion of the spleen suffices for the preservation of the protective power of the animal.

ii. The spleen and liver are the sites of formation of the agglomeratinins. At the commencement of immunization this activity is very great especially in the latter organ. With the passage of time after vaccination, however, agglomeratinin formation occurs notwithstanding splenectomy and destruction of liver function. On intraperitoneal implantation of liver or spleen in an immunized rabbit, agglomeratinin can be clearly observed ; the process is greater in the spleen than in the liver. Small injections directly into the parenchyma of the spleen or liver produce agglomeratinin formation more quickly than does intravenous vaccination. Investigation of the organ extracts of immunized rabbits shows that the spleen and liver are the chief sites of agglomeratinin formation.

W. Y.

i. MURAKAWA (G.). Lokale Immunisierung bei Trypanosomeninfektion. [**Local Immunization in Trypanosomal Infections.**] — *Fukuoka-Ikwadaigaku-Zasshi* (*Fukuoka Acta Med.*). 1930. Aug. Vol. 23. No. 8. [In Japanese. German summary pp. 64–65.]

ii. ——. Perorale Immunität gegen Trypanosomen. [**Peroral Immunity against Trypanosomes.**]—*Ibid.* [In Japanese. German summary p. 65.]

iii. ——. Partialantigen der Trypanosomen. [**Partial Antigen of Trypanosomes.**]—*Ibid.* [In Japanese. German summary pp. 65–66.]

iv. ——. Beiträge zur Kenntnis der Abwehrkraft des Trypanosoma-Immunserums gegen Infektion. [**Defensive Power of Trypanosome-Immune Serum against Infection.**]—*Ibid.* [In Japanese. German summary p. 66.]

v. ——. Kleine Versuche ueber embryonale Trypanosomen-Infektion. [**Small Experiments on Embryonal Trypanosome Infection.**]—*Ibid.* [In Japanese. German summary p. 67.] [Bact. Inst., Med. Faculty, Imperial Kyushu Univ., Fukuoka, Japan.]

i. The author has succeeded by the intraperitoneal injection of trypanosome vaccines (*T. equiperdum*, *T. gambiense* and *T. brucei*) in producing, in mice, rats and guineapigs, a local immunity. This immunity is specific and finally passes into a general immunity. In the early stages the antibody content of the peritoneal fluid, the omentum or spleen extract, is much greater than that of the blood serum. No phagocytosis was noted in the peritoneum of the immunized animals. The animals in which the great omentum had been extirpated developed no local immunity; hence the author considers this structure plays a great part in the production of this local immunity. Local immunity was similarly demonstrated in subcutaneous tissue and in the anterior chamber of the eye in rabbits.

ii. Although repeated oral administration of dead trypanosomes did not produce immunity, the author found that a feed of living trypanosomes, whether sensitized with bile or not, protected against a subsequent abdominal infection. But general immunity cannot be produced in this way.

iii. The protein obtained by the addition of ammonium sulphate to a watery solution of trypanosomes (*T. gambiense*, *T. equiperdum* or *T. lewisi*) acts as antigen and produces antibodies when injected intravenously in large doses into rabbits. The rabbit immune serum exhibits specific reactions, especially agglomeration, against the trypanosomes. Nothing of the nature of antigen was obtained in ether-acetone extractions of trypanosomes.

iv. The author investigated the rise and fall of the protective power of the serum of rabbits immunized against trypanosomes and against dead trypanosome vaccines. In each case the protective substance appeared between the 5th and 7th day, and rose slowly until it reached its maximum on the 10th to the 14th day. The fall in each instance was slow (70 days), but slower after trypanosome immunization than after vaccination.

Rabbits immunized with dead trypanosome vaccine and which, after six months, had completely lost their defensive power, and mice which had survived five months after vaccination, still proved immune on inoculation with the homologous trypanosome. From these facts the author concludes that in trypanosomal diseases the animals, notwithstanding the loss of active defensive power, still possess an active immunity.

v. The result of the author's observations is that trypanosomes do not pass the healthy placenta from mother to offspring. Microscopic examination of placentas of infected animals showed heavy infections in the maternal vessels, but none in the foetal. Preparations of embryos and new-born offspring of infected mothers were always negative.

W. Y.

ZIMMERMANN (Gerhart). Ueber die trypanozide Wirkung des menschlichen Serums im Tierversuch und in vitro. [**The Trypanocidal Action of Human Serum in the Animal Body and** *in vitro*.]—*Zent. f. Bakt.* I. Abt. Orig. 1931. May 4. Vol. 120. No. 7/8. pp. 422–440. [30 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

The author has repeated and confirmed the work of the reviewer and his colleagues on this subject [this *Bulletin*, Vol. 27, p. 237 and p. 804]. His conclusions are as follows :—

(1) The demonstration of YORKE, ADAMS and MURGATROYD that human serum exerts a direct trypanocidal action *in vitro* is confirmed. Human serum acts proportionately to its concentration.

(2) The hypothesis of ROSENTHAL and his colleagues, based on the repeated prophylactic treatment of mice with human serum before infection, that the trypanocidal action of human serum is indirect, has, as the result of further work, been found to be untenable.

(3) In icterus and liver disease the trypanocidal power of the serum is not completely lost, but only diminished so that the hypothesis of YORKE regarding the possibility of transmissibility of normally non-pathogenic trypanosomes to man is not supported by this work.

[Reference to Zimmermann's experiments on this subject shows that he worked with the serum of 6 cases of either catarrhal jaundice or of cirrhosis of the liver and with one case of pernicious anaemia. In each of the liver cases the trypanocidal action of the serum was greatly reduced. This subject has frequently been investigated by the *in vivo* method and the general results agree with those obtained by the reviewer and his colleagues in their *in vitro* experiments, viz., that in certain grave diseases of the liver the trypanocidal power of human serum may be completely lost.]

W. Y.

TRAUM (E.) & LINDEN (H.). Beitrag zur Frage der Genese der trypanociden Serumkörper beim Menschen an Hand klinischer Beobachtungen. [**The Genesis of the Trypanocidal Substance of Human Serum : a Communication based on Clinical Observations.**]—*Klin. Woch.* 1931. Aug. 8. Vol. 10. No. 32. pp. 1500–1501. [12 refs.] [Surg. Clinic & Hyg. Inst., Heidelberg.]

The authors commence their article with a mis-statement of fact when they write that the trypanocidal action of human serum is only manifest after injection of the serum into mice and that it is not demonstrable in the test tube. The reviewer and his colleagues have shown that the trypanocidal action of human serum is direct and is manifest in *in vitro* experiments and that the trypanocidal power is proportional to the concentration of human serum present ; and their work has recently been confirmed by ZIMMERMANN [this *Bulletin*, Vol. 27, p. 804 and above].

It is pointed out that relatively little is known regarding the nature and genesis of the trypanocidal substance, but that there exists a considerable mass of evidence to show that it is in some way bound up with the integrity of the liver since in certain severe diffuse liver lesions there is a great decrease or even total absence of serum trypanocidal substance.

In fact, ROSENTHAL and his colleagues have used the trypanocidal substance as a test for liver function, and it is recognized that this test may be positive when the sugar test and Kunfi's tetrachlorphenolphthalein or tetraiodphenolphthalein tests may be negative.

Details of a case in point are given. In this patient, who on subsequent post-mortem examination was shown to be suffering from Laennec's cirrhosis, the Kunfi test was negative, whereas the serum trypanocidal substance test was positive in that it was found to be markedly decreased in amount.

In a second case—that of a 7-year-old child suffering from severe haemolytic jaundice—the serum trypanocidal substance was considerably decreased; but a month after splenectomy it had greatly increased. In a third case—an 11-year-old child suffering from traumatic rupture of the spleen—the trypanocidal substance was found to be present in moderate amount 14 days after splenectomy and to have increased on the 55th day.

The authors conclude that if the liver is the chief site of formation of the serum trypanocidal substance, the spleen and remainder of the reticulo-endothelial system are sites of secondary importance.

W. Y.

REGENDANZ (P.). Ueber das Fehlen trypanozider Stoffe im Liquor cerebrospinalis des Menschen. [**The Absence of Trypanocidal Substance from the Cerebrospinal Fluid of Man.**]—*Zent. f. Bakt.* I. Abt. Orig. 1931. Feb. 23. Vol. 120. No. 1/2. pp. 89–93. [9 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

Since there have hitherto been only a few, and rather inadequate, observations on this subject, the author re-investigated it. His conclusions are :—

1. Neither in health nor in disease can trypanocidal substance be recognized by animal experiments in the cerebrospinal fluid of man.

2. Whilst human serum exhibits distinct trypanocidal action in mice experiments when administered in such doses as 0·1 or 0·2 cc., cerebrospinal fluid when given in 20 to 100 times the amount exerts no influence on the disease in mice infected with *T. brucei* or *T. rhodesiense*.

W. Y.

WALLACE (James Montague) & WORMALL (Arthur). **Red-Cell Adhesion in Trypanosomiasis of Man and Other Animals. II. Some Experiments on the Mechanism of the Reaction.**—*Parasitology.* 1931. July. Vol. 23. No. 3. pp. 346–359. [15 refs.] [Human Trypanosomiasis Inst., Entebbe.]

The following summary is given :—

" 1. The red-cell adhesion phenomenon in trypanosomiasis of man and other animals, first described by Duke and Wallace (1930) and shown by these authors to be due to the presence in the blood of the infected animal of a substance (adhesin) which appears during the course of an infection, has been investigated further. Several strains of *T. rhodesiense* and *T. gambiense* have been used for this study.

"2. Red-cell adhesion of this nature has been obtained with the red blood cells of primates only, thus confirming the earlier finding.

"3. No relationship appears to exist between red-cell adhesion and isohaemagglutination, or other types of haemagglutination. The removal, by absorption, of the α and β isohaemagglutinins from a human adhesin serum of blood group 0, or the removal from a monkey adhesin serum of agglutinins for baboon, rabbit and guineapig red cells does not lead to the removal of the adhesin.

"4. Centrifuging, *per se*, does not destroy to any appreciable extent the power of trypanosomes to adhere to red cells.

"5. Trypanosomes which have been freed from plasma by centrifuging and subsequent washing with citrate-Ringer-glucose solution give good adhesion with human or monkey red cells when a fresh adhesin serum or plasma is used. Little or no adhesion is obtained with these washed trypanosomes however, if the adhesin serum is very old or if it has been previously filtered through a Berkefeld filter candle or if the adhesin serum or plasma has been heated at 56° C. for 30 minutes.

"6. From this and other evidence the conclusion is reached that in addition to the red cells, trypanosomes and the adhesin some other factor (designated the 'X' factor) is necessary for red-cell adhesion.

"7. This 'X' factor is present in the serum or plasma of humans, monkeys, baboons, rabbits and guinea-pigs and has properties similar to those of complement. It is removed, as is most of the haemolytic complement, when the serum is filtered through a Berkefeld filter, it is destroyed by heating at 56° C. for 30 minutes, and, like haemolytic complement, it is inactivated when the serum is subjected to the action of dilute ammonia for about 1½ hours. Filtration, heating at 56° C. for 30 minutes and dilute ammonia appear to have no significant destructive action on the adhesin.

"8. The requirements for this red-cell adhesion phenomenon are (*a*) the red cells of a primate, (*b*) an adhesin, which is probably an antibody-like substance produced during infection with trypanosomes, (*c*) trypanosomes of a strain related to that which gave rise to the formation of the adhesin, and (*d*) a complement-like component ('X' factor) present in the plasma and serum of most, if not all, normal animals."

W. Y.

BRUSSIN (A. M.) & KALAJEV (A. W.). Die Bedeutung des Komplements und der Blutplättchen für die Feststellung der Thrombozytobarine. XXII. Mitteilung. [**The Significance of the Complement and Blood Platelets for the Demonstration of the Adhesion Phenomenon.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1931. Vol. 70. No. 5/6. pp. 497–521. [15 refs.] [Microbiol. Research Inst., Education Commissariat R.S.F.S.R. Moscow.]

The following summary is given :—

1. The chief factor necessary for regular results with the adhesion phenomenon is the quantity and quality of the complement.

2. The choice of blood platelets is determined by the complement which is employed, since, in order to obtain regular reactions, it is necessary to use complement and blood platelets from the same species of animal.

3. Washed platelets from the mouse cannot serve as indicators because their properties are changed by centrifuging and washing.

4. Accordingly, in order to ensure the appearance of the phenomenon, the method of Brussin and Belezki must be employed, i.e., the use of citrated blood of a normal mouse or citrated plasma of a guineapig, which furnishes both complement and platelets.

5. The use of various bacteria instead of platelets likewise suffices for a "loading" of trypanosomes and spirochaetes.

6. This loading occurs not only in the presence of specific serum, but also frequently in its absence.

7. Loading in the absence of specific serum is frequent in the case of certain bacteria (*B. coli comm.*), but rare in the case of others (*V. cholerae asiat.*).

8. Indeed with a culture of *V. cholerae asiat.*, it is not always possible to differentiate spirochaetal sera from trypanosomal sera.

9. These observations indicate the unsuitability of bacteria as indicators for the adhesion (loading) phenomenon.

10. Spirochaetes killed by heat can serve as antigen and give rise to the formation of thrombocytobarin in the serum of animals.

W. Y.

CORSON (J. F.). **Experimental Infection of Antelopes (Dik-Dik) with** *Trypanosoma rhodesiense.—Ann. Trop. Med. & Parasit.* 1931. Aug. 13. Vol. 25. No. 2. pp. 211–214. [2 refs.]

A number of experiments were made at Maswa, Tanganyika Territory, by direct inoculation of *T. rhodesiense* into small antelopes, called dik-dik, caught in a fly-free area.

The following are the conclusions and comments :—

" Four antelopes, dik-diks, were inoculated with *T. rhodesiense* and proved to be readily susceptible. Trypanosomes were numerous in the blood and posterior nuclear forms were present. The lymphatic glands became enlarged but gland puncture showed no trypanosomes. No evidence was obtained of infection of the central nervous system. The animals appeared to suffer little in general health during a period of about one month. In sheep and goats severe wasting is soon evident and numerous leucocytes and trypanosomes can be found in the cerebro-spinal fluid, often within a month from the date of inoculation. It does not appear that even selected resistant sheep may be used in experiments to represent antelopes as regards the question of a reservoir as the objection that sheep are not antelopes is unanswerable. These experiments were made mainly to see if the central nervous system became infected ; circumstances unfortunately curtailed the period of observation. No attempt was made to observe closely the behaviour of the trypanosomes in the antelopes.

" Observations over a longer period and under better health conditions than were possible at Maswa and on a larger number of animals are needed. Transmission by tsetse flies is of course required to get a closer resemblance to what may occur in Nature."

W. Y.

CORSON (J. F.). **Hyrax as a Possible Reservoir of** *Trypanosoma rhodesiense.—Jl. Trop. Med. & Hyg.* 1931. July 15. Vol. 34. No. 14. pp. 213–214. [1 ref.] [Sleeping Sickness Research Lab., Tinde, Tanganyika.]

Six specimens of hyrax caught on the rocks at Tinde, a fly-free area, were inoculated with *T. rhodesiense.* All became infected, the incubation period being usually 4 days. Trypanosomes were easily found in blood films, frequently several parasites being noticed in a field. Eight of the animals remained in apparent good health for more than a month. Subinoculation of rats was successful. Experiments showed that tsetse attacked hyrax in captivity readily.

The article concludes as follows :—

" *Comments.*—Hyrax is often seen in considerable numbers on rocky hills during the daytime, especially in the late afternoon and evening. Both

G. morsitans and *G. swynnertoni*, especially perhaps the former, attack man eagerly about this time. It seems probable therefore that hyrax is an animal on which they feed and, as it is so susceptible to infection with *T. rhodesiense*, the question of its serving as a reservoir of *T. rhodesiense* in sleeping sickness areas seems to be worthy of further investigation."

W. Y.

CORSON (J. F.). **Direct Infection of Native Fowls with** *Trypanosoma rhodesiense*.—*Jl. Trop. Med. & Hyg.* 1931. Apr. 15. Vol. 34. No. 8. p. 109. [2 refs.]

Five native fowls (Tanganyika) were inoculated in the muscles of the leg with blood of white rats infected with three strains of *T. rhodesiense*. Two fowls became infected. Trypanosomes were not seen in their blood but were transmitted to white rats in which they multiplied rapidly and showed posterior nuclear forms. The period of the fowls' infectivity was at least six weeks; they showed no impairment of health. The author suggests that these creatures might initiate an epidemic in man. [BRUCE, HAMERTON & BATEMAN (1911) in experiments involving 13 fowls and 1820 *G. palpalis* failed to obtain any evidence that the Uganda fowl could serve as a reservoir for *T. gambiense*.]

A. G. B.

CORSON (J. F.). *Trypanosoma rhodesiense* **in the Cerebrospinal Fluid of Sheep and Goats.** [Miscellanea.]—*Ann. Trop. Med. & Parasit.* 1931. Mar. 31. Vol. 25. No. 1. p. 145.

In the late stages of infection sheep and goats show nervous symptoms. Three goats and two sheep were killed by chloroform and the cerebrospinal fluid withdrawn by suboccipital puncture. Trypanosomes and a greatly increased cell count were found in all.

W. Y.

LE GAC (P.). Immunité observée chez *Cercopithecus lasiopyga petaurista* à la suite d'inoculation de *Trypanosoma gambiense*. [**Immunity in Cercopithecus sp. following Inoculation with** *T. gambiense*.]—*Bull. Soc. Path. Exot.* 1931. May 13. Vol. 24. No. 5. pp. 372–374.

Details are given regarding two *Cercopithecus lasiopyga petaurista* which were inoculated from human beings infected with *T. gambiense*. Trypanosomes appeared in the blood 40 and 45 days respectively after inoculation. In both animals the disease ran a severe course lasting 6 weeks to 2 months. Recovery then occurred and both animals were apparently immune to re-infection.

W. Y.

DAVIS (L. J.). **Experimental Feline Trypanosomiasis with Especial Reference to the Effect of Splenectomy.**—*Ann. Trop. Med. & Parasit.* 1931. Mar. 31. Vol. 25. No. 1. pp. 79–90. With 2 text figs. [20 refs.] [Wellcome Trop. Research Labs., Khartoum.]

As it has been shown that in domestic cats preliminary splenectomy exercises a most profound influence in aggravating the course of

experimental piroplasmosis (Davis, 1929), it was considered to be of interest to observe the effect of removal of the spleen on a subsequent trypanosome infection in the cat.

The following summary is given :—

" 1. Experimental *T. brucei* and *T. rhodesiense* infections have been observed in a small number of cats, some of which had been previously splenectomized.

" 2. Both strains of trypanosome produced sub-acute infections fluctuating in intensity and of variable duration.

" 3. The average survival period of the splenectomized cats did not differ significantly from that of the normal controls. The number of trypanosomes in the peripheral blood shortly before death appeared to be significantly higher in the splenectomized cats.

" 4. *T. rhodesiense* infections in normal and in spleenless cats inoculated by the intra-peritoneal route were compared with those in a similar series inoculated subcutaneously. No significant difference was noted in the duration or intensity of the infections in the two series.

" 5. Taliaferro's statistical method of analysing the nature of the resistance of the host was applied to the study of *T. rhodesiense* infections in a normal and in a splenectomized cat. In both cases the coefficient of variation indicated a state of continued reproductive activity of moderate degree."

W. Y.

DUBOIS (A.). Au sujet du metabolisme des trypanosomes. [**The Metabolism of Trypanosomes.**]—*Ann. Soc. Belge de Méd. Trop.* 1930. Dec. 31. Vol. 10. No. 4. pp. 445-448. [6 refs.]

The author summarizes briefly previous literature showing that trypanosomes utilize in their metabolism various sugars and alcohols. It appeared to him to be of interest to enquire whether these parasites can make use of monatomic alcohols, particularly ethyl alcohol. An account is given of the technique ; this did not differ essentially from that of previous workers. It was found that ethyl and methyl alcohols neither prolonged the life of the trypanosomes nor reanimated them as does glucose (Schern's phenomenon). Inosite likewise was without action : although this substance has the formula $C_6H_{12}O_6$, it is not a sugar, but a cyclic derivative found in muscle and of unknown significance.

W. Y.

MILLER (John W.). **Chagas' Disease in Panama : Report of Three Cases.**—*Southern Med. Jl.* 1931. July. Vol. 24. No. 7. pp. 645–647. [3 refs.]

The following summary is given :—

" (1) Three cases of Chagas' disease are reported, found for the first time in the Republic of Panama. All came from one focus in the basin of the Chagres River.

" (2) The trypanosomes found in the three cases are believed to be *T. cruzi.*

" (3) The trypanosomes disappeared spontaneously from the peripheral blood films without the action of any specific drug in the course of a few weeks. No opinion will be ventured regarding the final outcome of the attacks in these three children.

" (4) The symptoms and physical signs of Chagas' disease presented by these cases were essentially negative."

W. Y.

COLLIER (W. A.). Ueber Immunität bei der Chagaskrankheit der weissen Maus. [**On Immunity in Chagas' Disease in White Mice.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1931. Jan. 15. Vol. 112. No. 1. pp. 88–92. [2 refs.] [Robert Koch Inst., Berlin.]

Mice were infected with a strain of *T. cruzi* which had been weakened by previous treatment with trypaflavin. After intervals varying from 83 to 134 days the surviving animals were injected with the normal strain and watched for a further period of two months. They either remained negative or at most showed in their blood an occasional parasite.

There was thus produced not a sterilizing immunity, but a labile infection with immunity against superinfection. The immunity was not transmitted to the young either through the placenta or through the milk.

W. Y.

MAZZA (Salvador), ROMAÑA (Cecilio) & SCHÜRMANN (Krimhilda). Nuevas observaciones sobre la infección espontánea de armadillos del pais por el *Trypanosoma cruzi*. Hallazgo de este flagelado en *Dasypus novemcinctus*. Lin. del Chaco santafecino. Cuarta nota. [**Spontaneous Infection of Local Armadillos by** *T. cruzi*. **Its Presence in** *Dasypus novemcinctus*.]—*Prensa Méd. Argentina.* 1931. Feb. 28. Vol. 17. No. 27. pp. 1350–1357. With 8 text figs. [12 refs.]

The finding of *Dasypus novemcinctus* in the Argentine spontaneously infected with *T. cruzi* has been recorded previously (see this *Bulletin*, Vol. 27, p. 839); the author states however that, in many instances at least, the armadillo was not this species, but *Chaetophractus vellerosus vellerosus* (Gray), the identification having been faulty. He gives a list of the synonyms which have been given to *Dasypus novemcinctus*, Lin., 1758 down to 1905, fourteen in number, sufficient to satisfy the most ardent systematist. Nevertheless, this species does harbour the parasite, which was found in 2 out of 7 examined in Chaco and was transmissible to white rats and dogs. The Chaetophractus is a reservoir host in Jujuy, the *D. novemcinctus* being found infected once only in 150 examined in this district, but in Brazil, according to CHAGAS *D. novemcinctus*, *D. sexcinctus* and *D. unicinctus* are all found infected.

H. H. S.

BONACCI (Humberto). Nouveaux milieux de culture pour le *Trypanosoma cruzi*. [**New Culture Media for** *T. cruzi*.]—*C.R. Soc. Biol.* 1931. June 19. Vol. 107. No. 20. pp. 747–748.

The author has attempted to discover nutrient media more suitable for the culture of *T. cruzi* than are N.N.N., Noguchi's medium, Gaillard's medium and bouillon. He states the following three formulae have given satisfaction :—

Formula 1.—To 100 cc. of 1 per cent. gelatine melted at 50° C. and containing 1·5 gm. of peptone is added 1 cc. of a 50 per cent. solution of glucose and 5 cc. of the blood of a young guineapig. This medium is distributed in tubes which are slanted until it solidifies.

Formula 4.—Gelatine with 2·5 per cent. of peptone and 0·7 per cent. of sodium chloride. To this is added 1 cc. of a 50 per cent. solution of glucose

and 5 cc. of the blood of a young guineapig. Slants are made as in Formula 1.

Formula 9. As the previous, except that the proportion of peptone is 3 per cent.

W. Y.

WALLACE (J. M.). **Micro-Organisms in the Gut of** *Glossina palpalis.*—*Ann. Trop. Med. & Parasit.* 1931. Mar. 31. Vol. 25. No. 1. pp. 1–19. [20 refs.] [Human Trypanosomiasis Inst., Entebbe.]

CARPENTER (1912) described an apparent incompatibility between trypanosomes and "certain long bacilli" present in unstained preparations of the gut of *G. palpalis;* and PRATES (1928) observed the same thing. The author has re-examined the matter and has reached the conclusion that the bacteria noted by CARPENTER and PRATES are undoubtedly the "bacteroids," "symbionts" or "symbiotes" described by STUHLMANN (1907) and later by ROUBAUD (1919).

The distribution of the bacteroids is limited and they are easily missed in teasing-up the gut in the course of an ordinary dissection. They are "limited to a small portion, 3–4 mm. long, at the posterior end of that part which is relatively straight and narrow and is usually free from obvious blood." As noted by WIGGLESWORTH, the zone of giant cells containing bacteroids is far more localized than indicated by ROUBAUD; under favourable conditions it can be seen with the naked eye as an opaque patch which, with a hand lens, appears as an elongated white ring.

The author summarizes his work as follows :—

"1. Experiments are described which show why certain observers, who recorded the presence of 'long bacilli' in the gut of approximately 20 per cent. of wild *G. palpalis,* did not find these bacilli in *every* fly.

"2. Reasons are given for considering these 'long bacilli' to be identical with the intra-cellular bacteroids present in every fly, and therefore the incompatibility which these workers believed to exist between the 'long bacilli' and trypanosomes, is shown to be apparent only and due to the methods used in demonstrating the bacilli.

"3. Attempts were made to cultivate the bacteroids on various media though without success.

"4. 'Clean' laboratory-bred flies were fed on blood infected with known bacteria and the bacteria afterwards recovered in cultures from the gut of the flies. The duration of the 'infection' is shown to vary with different organisms and with some a point was reached when no further positive cultures were obtained. The longest time an 'infection' remained in a fly without killing it was thirty days.

"5. Evidence is given to show that tsetse-flies do not pick up bacterial infection even from grossly contaminated surroundings. The extreme cleanliness of the cages sometimes advocated in transmission experiments is therefore not essential.

"6. Cultures from numbers of flies show that during life the gut is apparently free from micro-organisms other than the bacteroids."

W. Y.

HORNBY (H. E.) & BAILEY (H. W.). **Diurnal Variation in the Concentration of** *Trypanosoma congolense* **in the Blood-Vessels of the Ox's Ear.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1931. Mar. 13. Vol. 24. No. 5. pp. 557–564. [3 refs.] [Vet. Lab., Mpwapwa, Tanganyika.]

The following summary is given :—

"(1) It can be shown that the normal distribution of *T. congolense*

within the blood vessels of its mammalian host is most uneven, the concentration being much higher in capillaries than in arteries and veins.

"(2) In the ear the average concentration of trypanosomes throughout the vessels is inversely proportional to the amount of blood passing through in unit time, *i.e.*, to the temperature.

"(3) This is reflected in blood-smears made from the ear veins, there being usually many more trypanosomes in the early morning than at midday.

"(4) Advantage of this knowledge should be taken in routine diagnostic procedures, and also when using blood-smears to measure the trypanocidal action of drugs."

W. Y.

MANSON-BAHR (P.). **The Epidemiology of Human Trypanosomiasis at the Present Time.**—*Proc. Roy. Soc. Med.* 1931. May. Vol. 24. No. 7. pp. 837–845 (Sect. Epidem. & State Med. pp. 25–33).

This is a general account of the subject and presents no new facts; it calls for no special notice here.

W. Y.

BROWNING (C. H.), COHEN (J. B.), ELLINGWORTH (S.) & GULBRANSEN (R.). **The Antiseptic and Trypanocidal Action of Certain Styryl and Anil Benzthiazole Derivatives.**—*Proc. Roy. Soc.* Ser. B. 1931. Apr. 2. Vol. 108. No. B 755. pp. 119–129. [5 refs.] [Med. School, Leeds; Path. Dept., Univ., & Western Infirmary, Glasgow.]

This paper is of a technical nature and should be consulted in the original by those interested.

W. Y.

CAMPOS (Ernesto de Souza). Une contribution de plus à l'étude de la transmission intra-utérine expérimentale du *Trypanosoma cruzi*.—*Bol. Soc. Med. e Cirurg. de S. Paulo.* 1930. Sept. Vol. 14. No. 7. [Summarized in *Rev. Sud-Américaine de Med. et de Chirurg.* 1931. June. Vol. 2. No. 6. p. 646.]

NÁJERA (L.). Sobre el tratamiento de la ceguera atoxílica en los tripanosomiásicos.—*Medicina Países Cálidos.* Madrid. 1931. Mar. Vol. 4. No. 2. pp. 104–107.

NÁJERA (L.). Observaciones sobre la valoración relativa de la triparsamida y del Bayer 205. Replica a los Drs. García Chico y Zschucke.—*Medicina Países Cálidos.* Madrid. 1931. July. Vol. 4. No. 4. pp. 299–314. [46 refs.] French summary (8 lines).

REGENDANZ (P.). Zur glykopriven Intoxikation bei der Trypanosomiasis usw. Erwiderung auf die vorstehenden Ausführungen des Prof. Schern.—*Zent. f. Bakt.* I. Abt. Orig. 1931. Jan. 20. Vol. 119. No. 5/6. p. 303. [1 ref.]

SCHERN (Kurt). Zur glykopriven Intoxikation bei der Trypanosomiasis etc. Erwiderung an Regendanz.—*Zent. f. Bakt.* I. Abt. Orig. 1931. Jan. 20. Vol. 119. No. 5/6. pp. 297–302.

YAWS AND SYPHILIS.

BLACKLOCK (D. B.). **Report on a Survey of Human Diseases in the Protectorate of Sierra Leone. Part I—Northern Provinces. Part II—Central and Southern Provinces.**—44 pp. 1930. Freetown.

In this interesting medical survey (which has been summarized elsewhere in this *Bulletin*), there are a number of references to yaws which it has been thought worth bringing together here; they have been put in tabular form.

	Northern Province.	Central and Southern Provinces.
Duration of survey ...	5½ months	12 months.
Population examined ...	4,337	5,153.
Yaws incidence (disease present or past)	In 24·7 per cent.	In 54 per cent.
Age incidence	Large proportion in children	Large proportion in children.
Primary lesion in 395 cases situated	Upper extremity 26 per cent. Lower extremity 54 per cent. Trunk, 13 per cent. (9 cases primary yaw occurred on penis) Head and neck, 7 per cent.	
Ainhum	3 male and 8 females, 10 of whom gave a history of yaws	7 males and 6 females of whom 6 males and 5 females gave history of yaws.
Goundou	2 cases, both females—history of yaws	5 cases, all males with a history of yaws.
Ganglion	4 cases	15 cases.
Arthritis	A large number of cases seen but etiology not ascertained	
Juxta-articular and subcutaneous nodules	306 among 2,904 persons	169 cases among 5,153 persons.
Subcutaneous nodules	The majority of the cases seen were apparently swellings due to Oncocerca infections and no differentiation of the true J.A.N. due to yaws or syphilis was made	
Lesions of the soles of the feet including "tender feet." Said to be a sequela of yaws		1,339.
Sabre tibia		38 cases, history of yaws in 31.
Gangosa...	64 cases among 2,924 persons	16 cases among 5,153 persons.

Although it is noted that a large proportion with sabre tibia gave a history of yaws the author does not seem to recognize that sabre tibia is a common lesion in yaws as he suggests it may be used as an index to gauge the incidence of congenital syphilis. It is worthy of note that among the population of 5,153 a single case exhibits a condition which

has been labelled "Hutchinson's teeth"; it would be interesting to hear more about this case.

The following further observations were made upon the 64 cases of gangosa occurring in the Northern Province:—

Sex and age incidence in 59 cases	0–10	3 male	1 female
	10–20	3	10
	21–30	8	15
	31–40	4	6
	41–50	1	7
	51–60	0	1
Nose alone affected (61 cases)		10	16
Mouth ,, ,, (61 cases)		2	6
Nose and mouth ,, (61 cases)		6	21
Positive history of yaws (53 cases)		14	32
Negative history of yaws (53 cases)		3	4

The lesion called gangosa was commonly associated with other lesions: the site of the first lesion and duration are given below as cited by the patient in 63 cases:—

Site.	Number of cases.	Duration in years.	
		Minimum.	Maximum.
Nose	24	9/12	20
Mouth, throat	9	1	12
Forehead	1	—	14
Ear	2	2	10
Malar region	1	—	4
Breast	3	2	3
Ribs	1	—	10
Clavicle	1	—	5
Arm	1	—	5
Elbow	1	—	8
Forearm	1	—	3
Hand	2	3	5
Iliac crest	1	—	25
Penis	1	—	1
Groin	2	6	8
Buttock	1	—	5
Knee	1	—	4
Leg	3	10	20
Ankle	3	9	10
Foot	4	2	20

It was observed that the ulceration process spreading from the angle of the mouth or nose invaded the cheek.

Deformation of eyelids, corneal opacities, keratitis, cataract, sabre tibia, absorption of small bones of fingers and toes so that the nail might rest on the metacarpal or metatarsal bones, were noted; gummatous swellings near joints were seen but joint seldom involved; lesions of the soles of the feet were few and mild.

H. S. Stannus.

KNOTT (James). **Yaws in Liberia.**—*Porto Rico Jl. of Public Health & Trop. Med.* 1931. June. Vol. 6. No. 4. pp. 385–390. With 6 figs. on 2 plates. [5 refs.] [Firestone Plantations, Liberia, W. Africa.]

The author considers yaws the most prevalent disease in Liberia and one causing more disability than any other. It is contracted in childhood and though the eruption may disappear after some months the disease remains latent during life causing stunting of growth, malnutrition and premature ageing. The lesions occurring among this people are those commonly seen in other endemic centres. The macular patches made up of minute papules were noted among the florid lesions. No lesion of mucous membrane nor iritis was seen. Gangosa, destructive joint lesions and periosteal nodes with bone pain were common. Crab yaws was very prevalent. Three cases of goundou in boys were seen, and juxta-articular nodules are common. Thickening of the skin of the palms of the hands and lichenification with depigmentation were also observed.

The author also refers to ganglion-like tumours about the tendons of the wrist and foot. "They consist of clusters of yellowish lobulated grain-sized masses of tissue adherent to fibrous trabeculae which arise within the tendon and emerge between its fibres."

Interstitial keratitis, cataract and optic atrophy were seen due to yaws lesions [but it is not quite clear what is meant]. Another lesion suspected as due to yaws was annular stricture just within the sphincter of the anus, which readily yields to treatment. Syphilis was not recognized to exist among this native population.

H. S. S.

LAMBERT (S. M.). **Yaws Incidence in the South Pacific.**—*Jl. Trop. Med. & Hyg.* 1931. May 1. Vol. 34. No. 9. pp. 117–122. With 1 text fig. [2 refs.]

A paper dealing with the incidence of yaws in the South Pacific Islands. The disease has certainly existed among these populations for some centuries. Formerly the entire population became infected. Syphilis is rare among these peoples as evidenced by the absence of chancre or scar of chancre among many thousands of natives of the various island groups examined [such evidence is, of course, by no means conclusive]. Dr. HARPER has only heard of two instances of the occurrence of syphilis in natives—one a Fijian male who contracted the disease from an Indian woman and it is interesting to note that he showed scars of yaws contracted in childhood and had suffered some late manifestations; the other a Solomon Islander who contracted syphilis on Rennell Island; in this case it may be inferred that he too had had yaws. Rennell Island, it is noted, is almost completely isolated and though yaws was found there last year nothing is noted as to the presence of syphilis. No other cases have been seen among natives by medical men though syphilis is extremely prevalent in the Indian communities of Fiji and the Asiatics in some other groups. The clinical characters of the disease are given as described by Dr. MONTAGU in the Annual Medical Report, Fiji, 1908, with special reference to the fact that a very large proportion of those treated at hospitals consisted of older children and adults suffering from lesions

which could not be distinguished from tertiary syphilis; common are crab yaws and a rather rapidly spreading ulcerative nodular lesion which may cover large areas of skin with cicatrization in its wake and also involve mucous membranes. Periosteal nodes are also common and indurated masses in the body of a muscle and in the tongue are described as due to yaws—they disappeared under iodides. During the past 20 years, of 182 Melanesians and Polynesians admitted, 42 had died of G.P.I.; "none of this number had syphilis." Aneurism and aortic disease are common.

The second half of the paper deals with figures and some of the results of campaigns directed against yaws; treatment was by salvarsan.

H. S. S.

TODD (K. Waller). **Halarsol in Yaws.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1931. June 30. Vol. 25. No. 1. pp. 65–74. [9 refs.]

A paper announcing results obtained by the author in 1929 and in 1927 (with Dr. CHESTERMAN).

The maximum dose which does not cause vomiting was considered to be the best; this was apparently about 4 cc. of a 2·5 per cent. solution given intravenously in adults and 1–2 cc. intramuscularly in very small children; the subcutaneous route is too painful to be practicable.

Note is made that the drug is liable to develop extreme toxicity on exposure after the ampoule is opened. The results of treatment extracted from this paper and put in tabular form are as follows:—

(C = cured; R = relapse; F = failure.)

Single injection series:						
14	with secondary rashes	followed for	6 months	11 C	3 R	
10	,, ,,	,,	2 ,,	10	–	
10	,, late secondaries	,,	6 ,,	4	6 F	
Two injection series:						
13	with secondary rashes	followed for	6 months	11 C	2 R	
13	,, crab yaws	,,	3 ,,	9	4 F	
10	,, hyperkeratosis	,,	5 weeks	8	2 F	
4	,, tertiary ulcers	,,	3 months	3	1 F	
Three injection series:						
21	with late secondaries			13 C	8 F	

No serious accident occurred though 1,731 injections were given. The W.R. in 4 cases became negative after 1, 2, 3 and 3 injections; in two cases it remained positive after 3 and 6 injections.

The author considers that Halarsol "may be the drug of election for rapid sterilization of yaws" [a claim that the reader will not consider justified].

H. S. S.

VAN NITSEN. Le pian congenital. [**Congenital Yaws.**]—*Ann. Soc. Belge de Méd. Trop.* 1930. Dec. 31. Vol. 10. No. 4. pp. 482–486.

The author comments on the paucity of facts suggesting that yaws may be inherited, and in recent literature has only seen those articles by BANDGAPADHYAY, LEON, WILSON and MATHIS summarized in a previous number of this *Bulletin*. He supports the view therein

expressed by the reviewer that the evidence produced did not in any way support the thesis that heredo-yaws occurred. His own experience leads him to state categorically that a woman with a history of past yaws or with signs of active disease never gives birth to a child with yaws. A child is never born possessing an immunity to yaws. On every occasion that a child has exhibited any stigmata, a syphilitic infection has been traceable.

H. S. S.

DEIBEL (H. Kellermann) & ELSBACH (E. M.). Lichen framboesiacus (pian dartre). [**Framboesial Lichen.**]—*Geneesk. Tijdschr. v. Nederl. Indië.* 1931. July 1. Vol. 71. No. 7. pp. 675–689. With 7 figs. (4 coloured) on 6 plates. [29 refs.] [Military Med. Hosp., Batavia, Java.]

A detailed description of this micropapular eruption which is a very typical secondary manifestation in yaws. The differential diagnosis from other lichenoid affections (lichen pilaris, syphiliticus, scrophulosorum ; lichen ruber acuminatus, nitidus and trichophyticus) is dealt with in detail. The eruption consists of disseminated areas of depigmented keratotic micropapulae arising from the hair follicles.

Histologically slight infiltration, but marked hyperkeratosis and depigmentation are the characteristic features. From an anatomo-pathological point of view, this picture is nearly pathognomonic.

W. J. Bais.

FAST (G.). Oogziekten bij framboesia tropica, naar aanleiding van een geval van neuroretinitis. [**Eye Diseases in Yaws ; a Case of Neuroretinitis.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1931. Apr. 1. Vol. 71. No. 4. pp. 361–372. With 13 text figs. [12 refs.]

A Javanese woman of 20 during pregnancy suffered from an acute neuroretinitis of the right eye. Within a week of the first administration of arsphenamine the progress of the affection was arrested and considerable improvement followed during further treatment ; yet an important defect of the optic field remained. The patient had suffered from yaws 17 years before and showed typical scars of this affection. Syphilis could be excluded (absence of other syphilitic symptoms, birth of a healthy child, long latency of the disease, prompt reaction to arsphenamine, negative Wassermann test in the husband's blood), as well as other possible causes of retinitis (nephritis, tuberculosis). The author ascribes the affection to yaws and quotes the literature in regard to the connexion of eye diseases with yaws, arriving at the conclusion that such affections are apparently rare but might be observed more frequently if proper attention were paid to the possible aetiological connexion. Apart from dermal lesions round the eye, yaws may cause conjunctivitis, a certain type of pterygium, orbital periostitis, cyclitis, and iridocyclitis, parenchymatous keratitis and neuroretinitis.

W. J. Bais.

BROSIUS (O. T.). **Yaws—Case Reports.**—*Nineteenth Ann. Rep. Med. Dept. United Fruit Company, Boston, Mass.* 1930. pp. 108–109. With 1 text fig. [United Fruit Company Hosp., Almirante, Panama.]

A short note upon 4 typical cases of yaws seen at the Almirante Clinic, Panama, during the year. Only 12 cases have been observed during the 5 years past.

H. S. S.

*BUTLER (C. S.). **Diagnosis and Treatment of Yaws.**—Reprinted from *Internat. Clinics.* 1930. Ser. 40. Vol. 2. 14 pp. With 18 figs. (1 coloured) on 8 plates. [15 refs.]

The author starts with a definition of yaws from DE SAUVAGES (1763). From 1530 when FRACASTORO named syphilis down to SYDENHAM (circ. 1666) and on to the time of DE SAUVAGES there was apparently no question as to the identity of yaws and syphilis. After the last-named author "certain groups of symptoms were set off by the authorities and described under the name of yaws" and by 1803 this idea was well planted in the literature. Since then doctors have gone to the tropics educated to believe that yaws is distinct from syphilis. The supposed differences however "all vanish into thin air when brought into the spotlight of a critical interrogation."

The author proceeds by a "yaws catechism," a brief question and a detailed reply. To the question, If yaws is syphilis why is it not congenital ?, he replies that it is, and that the statement that it is not is due both to insufficient observation and to the signs of congenital syphilis having been excluded by definition. The extra-genital position of the initial lesion is explained by its, as a rule, innocent acquirement. Among filthy people subject to overcrowding syphilis is predominantly innocent. For the same reason it is a disease of childhood, and the fact that it is a disease of childhood explains the relative infrequency of congenital yaws.

To the question why mercury does not cure yaws he replies that it does, giving a reference to HUNT and JOHNSON [*U.S. Nav. Med. Bull.* 1923, Vol. 18, p. 599. "Mercury internally has been thought to do good in some cases."] The relative value of mercury, bismuth and the organic arsenicals in the treatment of trepanematosis is given as 4 to 7 to 10.

To the question why yaws fails to show vascular diseases and gummata of the internal organs he replies that it does.

To the question why yaws is not seen in temperate climates, he replies that it is seen, cases being not at all infrequently published at the present time. On the initial lesion and its difference from the Hunterian chancre OSLER is quoted to the effect that extragenital chancres are less likely to manifest induration and more given to phagedena and oedema. The author has, however, seen "several initial yaws lesions which showed the induration typical of the Hunterian chancre."

On the immunity question he says that yaws immunizes to syphilis both in man and monkey (SCHÖBL). He thinks, however, experimental animals will fail to convince us of the unity of the two diseases because none of them give reactions comparable to those of man in response to inoculations of the virus. JAHNEL and LANGE proved that in general paretics *T. pallidum* immunizes to *T. pertenue* [this *Bulletin*, Vol. 26. p. 175]. To the question why, if yaws is syphilis, there is so little tabes and G.P.I. among natives who suffer from yaws, the reply is that in syphilis-affected natives too these sequelae are rare.

He now defines yaws as "epidemic non-venereal syphilis transmitted innocently among primitive peoples" constituting under stone-age conditions of personal hygiene one of the exanthemata of childhood.

A. G. B.

---

* This paper has been already reviewed [*ante*, p. 439]. Captain Butler, however, considers that the former review was critical rather than informative, and that he was misrepresented in it. An attempt has therefore been made to summarize his paper without omitting anything that appears essential to his argument.

ARNAUD (A.), FORNARA, VIGONI & VAN HOOF. Syphilis et pian seraient-ils une seule et même affection ? [**Are Yaws and Syphilis Identical ?**]—*Bruxelles-Méd.* 1931. Apr. 19. Vol. 11. No. 25. pp. 722–735.

In reply to an enquiry formulated by the *Bruxelles-Médical* the opinions of doctors Arnaud, Fornara, Vigoni and van Hoof are now given upon the identity or otherwise of yaws and syphilis.

The first mentioned quotes some of the findings of other writers without adducing any new facts. Fornara alludes to the pitfalls in interpreting cross immunity experiments. He himself has seen clinical yaws developed in a man before infected with syphilis and *vice versa,* and has seen syphilis contracted by persons suffering from active and latent yaws. He believes the cerebrospinal fluid is always negative for W.R. in yaws. Vigoni produces geographical distribution as evidence : in Lusanga area of Kwilu where 100 per cent. natives were infected with yaws, white occupation has recently begun with the introduction of syphilis and this yaws-infected population shows no immunity to syphilis. Van Hoof deals with the lesions common in syphilis which are not seen in yaws.

H. S. S.

CONNOLLY (P. P. D.). **Do Yaws and Syphilis confer Immunity against Each Other, and if so to what Extent ?**—*Kenya & East African Med. Jl.* 1931. Mar. Vol. 7. No. 12. pp. 345–348. With 2 diagrams on 1 plate.

The author was struck by the uneven and patchy distribution of yaws and syphilis in the various provinces of Kenya and attempts to find an explanation for this and for the fact that " where yaws is found in abundance syphilis is rare and *vice versa.*" To this end he examined the numbers of admissions due to yaws and syphilis for Kikuyu and Kavirondo natives into the Infectious Diseases Hospital, Nairobi.

He found that " syphilis was five times more frequent among the Kavirondo than amongst the Kikuyu " and that " malignant syphilis was three times more common in the Kavirondo," and conversely " the yaws rate in the Kikuyu outnumbers that in the Kavirondo by nearly three hundred per cent. . . . . Framboesia maligna in the Kikuyu is relatively common ; in the Kavirondo it is absent." Dr. Connolly then says, " These figures if they do not prove an immunity between the two diseases at least strongly suggest it." Further, he has " only known about two cases where a patient having suffered from yaws has subsequently contracted syphilis " and he has " not come across a case where a patient having had syphilis had subsequently contracted yaws. The immunity between the two would seem to be of a high degree though it is almost certainly not absolute."

[While such speculations may be useful in helping others to keep an open mind, they must remain speculations pure and simple. The evidence adduced has no statistical value whatever. Dr. Connolly suggests that a preparation like luetin which might be called framboesin could possibly be prepared and might give interesting results. Actually such a preparation has been made and so named.]

H. S. S.

BURKE-GAFFNEY (H. J. O'D.). **The Clinical Value of the Combined Kahn and Wassermann Tests in the Tropics, with Special Reference to Yaws and Syphilis.**—*Jl. Hygiene.* 1931. Apr. Vol. 31. No. 2. pp. 215–224. [20 refs.] [Med. Lab., Dar-es-Salaam.]

Of the 500 sera tested the clinical condition was known in 448 cases. An exact agreement was found between the tests in 96·4 per cent. of all cases. The investigation proved the reliability of the Kahn test in the tropics and the keeping properties, at room temperature, of the only special reagent required in that test—cholesterinized antigen. It is recommended that when both tests are available they should be performed in parallel.

W. F. Harvey.

LACAPÈRE (G.). L'influence du paludisme sur la syphilis chez l'Arabe. [**Influence of Malaria on Syphilis in the Arab.**]—*Rev. Prat. Malad. des Pays Chauds.* 1930. Aug. & Oct. Year 9. Vol. 10. Nos. 8 & 10. pp. 386–388; 471–473. [1 ref.]

In view of the efficacy of malarial therapy in general paralysis many have speculated upon the possible part malaria may play in endemic areas upon the incidence and course of syphilis among natives. Dr. Lacapère during three years spent in Morocco has looked for evidence upon this question.

In the first place he quotes the case of an Arab woman who for several months suffered a rise of temperature to 39° C. each evening till four the following morning, of a typically quotidian malarial character, which ceased after the third injection of N.A.B., exhibited as the result of her blood and that of her husband giving a positive W.R. while she herself showed no symptoms of syphilis. This is a secondary syphilitic fever impressed with the character of a malarial intermittent pyrexia. [Blood apparently not examined for malarial parasites.] Apart from some similar observations malaria would appear to have no effect upon secondary syphilis. While GÉMY has affirmed that malaria has no effect on the virulence of syphilis, Lacapère believes that malaria is the principal cause of tertiary syphilis causing the markedly mutilating lesions in the skin and osseous system seen among Arabs. Ulcerative lesions of the skin form 60 per cent. of the tertiary skin conditions seen at Fez and bony lesions are about as frequent. The author believes that the malarial cachexia so common among these peoples causes an arterial hypotension, often so low as to suggest adrenal insufficiency, and that the stasis so engendered allows groups of spirochaetes to set up the necrotic lesions in the skin. At the same time the intense loss of red cells, almost suggesting a pernicious anaemia, puts such a strain upon the bone marrow that the bone falls a victim to the syphilitic virus.

FOURNIER showed that Europeans suffering from chronic malaria were liable to malignant extensive ulcerative lesions liable to become phagedenic and again that an attack of malaria would precipitate an explosion of ulcerative skin lesions and bone affections.

[Colonel HARRISON has supplied the following interesting comment:

"With regard to the possibility of malaria being the principal reason for tertiary syphilis causing severe mutilating lesions in Arabs, a case related by W. H. GOECKERMANN (*American Jl. Med. Sci.*, 1928, v. 175, 261) is interesting. A woman five months after malarial treatment of

G.P.I. developed a nodular cutaneous syphilide. The malaria had caused a complete remission of the G.P.I. GERSTMANN ('*Die Malariabehandlung der Progressiven Paralyse,*' 2nd Ed., p. 216) cites four cases reported by MARKUSZEWICZ, SCHULTZE, PFEIFFER and KIRSCHBAUM in which gummata developed after malarial treatment of G.P.I. and one in WAGNER-JAUREGG'S clinic which developed a syphilitic arthritis. GERSTMANN, like GOECKERMANN, seems to favour the hypothesis that malarial treatment makes the supporting and vascular structures allergic.

"As to the immediate cause of syphilitic ulceration, in a recent paper by WILE, WIDER and WARTHIN (*Am. J. Syph.* 1930, v. 14, 1) relating a case in which innumerable ulcers occurred it was reported that microscopic sections showed the lesions to be due to severe endarteritis and closure of cutaneous vessels, resulting in necrosis of the tissues supplied. No spirochaetes were found in the necrosed areas, and WARTHIN regarded them as infarcts. It seems possible that fever may act in two ways : (1) as an agent which is noxious to and temporarily stimulates the spirochaetes to increased activity, on the Jarisch-Herxheimer principle and (2) by stimulating the defensive reaction of the body (allergy), including in this increased perivascular infiltration which results in closure of vessels and necrosis of parts supplied. As to (2) probably it is right to say that, in most cases, syphilis kills through the defence put up by the tissues."

The course run by a syphilitic infection is well known to be influenced by other factors. Women often show the first clinical sign of syphilis after the menopause and this fact may be due to the reduction, or stoppage, of ovarian hormones. The well-known mildness of syphilis in females is confined to the sexually active period, and another interesting fact is that syphilitic lesions have been found in the ovary only very rarely.

Lacapère also is among those who see in chronic malarial infections among natives a possible cause for the rarity of general paralysis among them. With regard to this theory, it is worthy of note that in certain races, NAGELSBACH (see *Bulletin of Hygiene,* 1926, p. 867) showed that neurosyphilis is unknown in parts of W. Abyssinia where syphilis is rife but malaria non-existent.]

H. S. S.

BRUNSTING (Louis A.). **Syphilitic Juxta-Articular Nodes.**—*Amer. Jl. Syph.* 1931. Jan. Vol. 15. No. 1. pp. 42–49. With 1 plate. [4 refs.] [Mayo Clinic, Rochester.]

The author gives the following summary :—

"Clinical and histopathologic descriptions are given of juxta-articular nodes occurring in the cases of three men who had never been in the tropics. Definite evidence of syphilis was present in each case ; in two cases there was history of infection. The Wassermann reaction of the blood was uniformly positive. In two of the cases there were concomitant signs of visceral involvement : cardiovascular syphilis in one case, and cardiovascular and neurosyphilis in the other. Response to treatment for syphilis was surprisingly prompt and complete in the one case in which the juxta-articular nodes presented the only clinical sign of the disease. In the second case, the solitary nodule was excised for histologic study ; in the third case sufficient time had not elapsed to permit of evaluation of response of the nodules to treatment. Microscopic evidence of syphilis was definite only in one case ; in the other cases the cellular reaction was nonspecific."

In case one the lesions consisted of 7–8 discrete, firm, moveable, slightly tender, subcutaneous tumours a half to two centimetres in diameter distributed on the flexor surface of the fingers and palm of the right hand, unattached to skin or to tendons. These all practically disappeared in 6–7 months under intensive anti-syphilitic treatment.

The second patient presented a single subcutaneous tumour 2 cm. in diameter just below the left olecranon crest. A portion of the tumour was removed for investigation; the remainder disappeared under treatment.

The third patient showed on the palmar surfaces of the fingers of both hands numerous firm fibroid slightly moveable painless subcutaneous nodules ½–1 cm. in diameter and only apparent on palpation. Below the left olecranon also 3 small nodules were found: others had existed but disappeared spontaneously according to the patient.

"The histopathologic characteristics in the three cases herein described consisted essentially of ill-defined nodules of fibrosis in the middle part of the cutis and subcutaneous tissue, with a central zone of vascularity. The inflammatory reaction was chiefly perivascular in distribution and the infiltration consisted largely of lymphocytes and plasma cells. Proliferative changes in the blood vessels were not of marked degree. In only one case were the histopathologic changes of sufficient degree to warrant the diagnosis of syphilis on microscopic examination. In the other cases, the microscopic appearance was that of fibrosis with a cellular reaction, chronic inflammatory in character, and of a nonspecific type."

H. S. S.

FONTOYNONT (M.), GIRARD (G.) & WOLTZ (H.). Nouvelle conception pathogénique des "nodosités juxta-articulaires" des Malgaches, avec les déductions qu'elle comporte. [**New Pathogenic Conception of J.A.N. in Malagasies.**]—*Bull. Soc. Path. Exot.* 1931. Mar. 11. Vol. 24. No. 3. pp. 209–214. [1 ref.] [Pasteur Inst., Antananarivo.]

After referring to the still uncertain etiology of J.A.N., the authors remark upon the invariable presence of a white substance like zinc ointment in all the nodes when they show signs of softening, but before ulceration, that came under his notice at Antananarivo in Madagascar. This creamy substance contained few if any cellular elements but showed in earlier cases a tangled mass of needle-shaped crystals; in older cases which were harder to the touch the crystalline elements were absent and replaced by a more desiccated chalky paste. These contents of the nodes were all sterile on cultivation. In three cases [no clinical description given] small nodes were noticed on the pinna which immediately suggested tophi. These resembled in their histological picture the nodes on the limbs of the patients and the account originally given by JEANSELME [no histological description given], and their contents macroscopically resembled the contents of the J.A.N. and proved on chemical analysis to consist of uric acid, cholesterin and salts (phosphates and chlorides of sodium, calcium and magnesium) in the proportions 56 : 13 : 21, but no tyrosin. It will be remembered that CAROUGEAU considered the crystalline deposits in J.A.N. to be tyrosin but it is possible his test did not distinguish between cholesterin and tyrosin.

The presence of uric acid suggested estimations of uric acid in the blood serum and these patients showed a figure around 12 cgm. per litre or three times the normal for Europeans, supporting the idea of a gouty diathesis for J.A.N. It was found, however, that the uric acid-urea ratio, normally 0·03 in Europeans, was among the general Antananarivo population 0·05 and that this same figure was true for the J.A.N. cases. Uric acid calculus is common, but blood cholesterol is low in Madagascar as among other races in the East.

In one case which came to necropsy a fistula was found leading down to a tuberculous left ankle joint (proved by guineapig inoculation).

The authors suggest that they have been dealing with cases of tubercular

infection with attenuated virus or a tuberculous "ultra-virus." They ask what part may a tuberculous infection play in the genesis of J.A.N. Is it an inconstant epiphenomenon ? Is it a primary cause acting in the presence of a special soil ?

H. S. S.

CLIMATIC BUBO AND LYMPHOGRANULOMA INGUINALE.

NAUMANN (H. E.). Der klimatische Bubo und seine Therapie. [**Climatic Bubo and its Treatment.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1931. Mar. Vol. 35. No. 3. pp. 181–184.

The author relates the occurrence of six cases, all members of a ship's company who gained their infection from the same woman at the port of Jéremie (Haiti). All presented the now well-known penile lesion, in the first case three days after coitus. Gland enlargement occurred on the 6th day. All had fever and splenic enlargement. All investigations as to etiology were negative. Treatment consisted in solganol 0·01 to 1·0 gm. intravenously every second day. In the first, the earliest case, gland enlargement and penile lesion had disappeared on the 14th day of treatment. In the most advanced case and that having longest interval since infection, resolution was obtained in 6 weeks. They were all what might be called early cases and softening had not taken place in any nor did it take place subsequent to treatment being commenced.

The lady was then apprehended. She appeared to be in excellent general health. There were some small palpable glands in the inguinal regions. Leucorrhoeal discharge was abundant but negative for gonococci. No chancre present, but on the cervix there was an erosion, and the mucous membrane about the vaginal opening was covered with white spots.

In using solganol watch must be kept on the urine ; albuminuria in some degree was always produced.

H. S. Stannus.

REZENDE (Motta) & SOBRINHO (J. Muniz). Iodurêto de sodio na linfogranulomatose inguinal sub-aguda. [**Sodium Iodide in Climatic Bubo.**]—*Arch. Brasileiros de Med.* 1931. Jan. Vol. 21. No. 1. pp. 1–5.

Intravenous injection of iodine in the treatment of this condition is not new, 10 cc. of Lugol's solution with an equal quantity of normal saline having been employed as a daily injection by RAVAUT. The authors, however, use the sodium salt, 10 cc. of a 10 per cent. solution, and regard it as specific.

They record the case of a man of 23 years with enlarged groin glands of some months' duration, with exacerbations and remissions. Various forms of treatment were unavailing, among them a course of neosalvarsan, the W.R. being positive. The first injection of the sodium iodide was followed by a rise in temperature to 40·3° C. (it had till then been fluctuating between 36·6° and 39° C.) ; this fell to 36° next day, rose to 36·6° for another 24 hours and then remained at 36° for the ensuing 6 days during which he was kept in hospital. The "swollen glands became markedly reduced after the injections and his general state improved considerably" state the authors, but unfortunately no mention is made of the number of injections given.

H. H. S.

FREI (W.) & WIESE (J.). Zur Behandlung der Lymphogranulomatosis inguinalis, insbesondere mit einem Kupferpräparat. [**Treatment of L.I. especially with a Copper Preparation.**]—*Klin. Woch.* 1931. Feb. 28. Vol. 10. No. 9. pp. 404–406. [Municipal Hosp., Berlin-Spandau.]

The author has tried a copper preparation "Cuprasol H" in the treatment of L.I. 1·5 cc. of the solution as put up in ampoule up to 2·5 or 3·0 cc. may be given intravenously twice weekly or smaller doses more frequently. Watch must be kept on the albumin and bile pigments in the urine. Cuprasol is not very effective alone, but in conjunction with stibenyl gives good results. Every second day an injection is given, alternately cuprasol and stibenyl—8 to 10 of each, 3 to 4 weeks witnessing in most cases a cure.

H. S. S.

HELLERSTRÖM (Sven). Zur Kenntnis der Hautallergie beim Lymphogranuloma inguinale. [**Skin Allergy in Lymphogranuloma Inguinale.**]—*Klin. Woch.* 1931. Mar. 28. Vol. 10. No. 13. pp. 595–597. [9 refs.] [Karolin Inst., Stockholm.]

FREI introduced his now well-known specific cutaneous test for L.I. at the end of 1925. Since then its use has been repeatedly demonstrated by various observers, chiefly in Germany and Scandinavia. The preparation of the antigen and method of performing the test, however, require care and various precautions must be taken if successful and correct results would be obtained. These are set forth in this paper and should be studied by all those interested since it cannot be summarized.

H. S. S.

LEVADITI (C.), RAVAUT (P.), LÉPINE (P.) & SCHOEN (R.). L'affinité d'un virus isolé de la lymphogranulomatose inguinale (maladie de Nicolas et Favre) pour le système lymphatique du singe. [**Affinity of Lymphogranuloma Virus for Lymphatic System of Monkey.**]—*C.R. Acad. Sci.* 1931. June 15. Vol. 192. No. 24. pp. 1600–1602. [1 ref.]

Following their previous work by which an ultravirus had been demonstrated in man suffering from L.I., the authors have carried out researches to demonstrate its affinity for lymphatic glands in monkeys, animals which can be successfully inoculated as shown by HELLERSTRÖM and WASSÈN. Using as the inoculum an emulsion of brain substance from a monkey which had died seven days after subdural infection, injection into the inguinal gland of another monkey was followed by local swelling and a general polyadenitis. After an early diminution there was a recrudescence of signs on the twentieth day without symptoms of illness. Thirty-one days later a gland from the opposite inguinal region was excised, emulsified in isotonic saline and inoculated intracerebrally into a third monkey. After showing signs of paralysis of the limbs the animal died on the twenty-fourth day with P.M. signs of a meningo-encephalitis, but cultures were negative.

The histological changes in the glands of the second monkey were typical—marked endothelial proliferation of vessels with intense monocytic and basophilic infiltration.

H. S. S.

LEVADITI (C.), RAVAUT (P.), LÉPINE (P.) & SCHOEN (R.). Présence du virus de la lymphogranulomatose inguinale (maladie de Nicolas et Favre) dans les organes des singes inoculés par voie intracérébrale. [**Presence of Virus of L.I. in the Organs of Monkeys inoculated Intracerebrally.**]—*C.R. Soc. Biol.* 1931. July 3. Vol. 107. No. 22. pp. 959–961. [2 refs.]

Two papers by these authors have recently appeared in connexion with this work. In the present communication are given their findings as regards the presence of the ultra-virus in various organs of a monkey killed when in the last stages of an L.I. infection produced by intra-cerebral inoculation. Emulsions of various organs were inoculated intracerebrally into a number of clean monkeys. The liver, spleen, kidney, marrow, and lymphatic glands were demonstrated to contain the virus while the blood was negative. No changes are mentioned as occurring in these organs, but in all the animals the characteristic meningitis with perivascular lymphoid infiltration was produced.

H. S. S.

HELLERSTRÖM (Sven) & WASSÈN (Erik). Meningo-enzephalitische Veränderungen bei Affen nach intracerebraler Impfung mit Lymphogranuloma inguinale. [**Meningo-Encephalitis in Monkeys after Intracerebral Inoculation with L. I.**]—VIIIe Congrès International de Dermatologie et de Syphiligraphie, Copenhague 5 au 9 août 1930. 5 pp. With 9 figs. (8 coloured).

Intra-cerebral injection of suspensions of L. I. gland tissue 1 : 50 to 1 : 100 in physiological saline, after filtration through gauze, in doses of 0·04, 0·06, 0·08 cc. produced in Rhesus and Cynomolgus monkeys a meningo-encephalitis. The suspension was prepared from glands in typical cases of L. I. of 3 weeks' standing. After an incubation period of 6–12 days the monkeys became somnolent and later exhibited ataxia and clonic spasms. Some died after 6, 14 to 27 days ; others were killed at similar intervals. Post mortem examination revealed a generalized lepto-meningitis involving cerebellum as well as cerebrum and was marked around the plexus and most in evidence in the sulci. Excellent coloured plates show the hyperaemia, the infiltration, especially perivascular with endothelial cells and polymorphonuclear leucocytes. Passage from monkey to monkey was successful to the 2nd in Rhesus but up to the 11th in Cynomolgus.

Intra-preputial inoculation was done in one monkey. In thirteen days the inguinal glands were enlarged to the size of peas and the cellular reaction found on section was similar to that in the brain and to that found in early cases in man.

The meningo-encephalitic changes resembled those seen in monkeys caused by vaccinia virus and therefore cannot be said to be specific but they are, there is strong ground to believe, caused by the virus of L. I. and this is borne out by the reactions carried out according to Frei's method. Attempts to demonstrate the virus microscopically or by cultural methods failed.

H. S. S.

LATKO (N.) & MICHAILOW (S.). Zur Ätiologie des Lymphogranuloma inguinale. [**Etiology of Lymphogranuloma inguinale.**]—*Dermat. Woch.* 1931. Mar. 7. Vol. 92. No. 10. pp. 349–353. With 4 text figs. [8 refs.] [Dermato-Venereal Clinic, 2nd Univ., Moscow.]

Writing from the clinic for skin and venereal diseases, Moscow, the authors describe a case of L. I. with fever and general symptoms—a 34-year-

old peasant from Njeshin, married 15 years, with history of gonorrhoea 3 years before but otherwise no venereal history previously and none in family: he denied recent extra-marital coitus. Five months before coming under observation he noticed a node on the prepuce which soon developed into a painful ulcer with hard edges, gray sloughy base and a small ring of inflammatory exudation around. Two weeks later the right inguinal glands swelled and in another week the left side was affected. When seen there were masses the size of eggs in each groin and masses of glands in each iliac region, the size of an infant's head on the right side, on the left side rather smaller, hard and painful to pressure.

Blood examination showed W. R. negative, R.C. 5,100,000; W.C. 5,500; Haemoglobin 65 per cent. Differential count about normal. Skin von Pirquet weakly positive. Ulcer and gland juice negative for Ducrey's bacillus or spirochaetes. Culture and inoculation into guineapigs negative for tubercle. By culture two organisms were isolated from gland puncture juice, one the hay bacillus, the other a diphtheroid avirulent to guineapigs. A vaccine was made from the latter and 22 injections given during the four months the patient took to get well.

The authors point out that the organism described by KITCHEVATZ and PETROWITSCH had practically the characters of the hay bacillus and though they do not wish to say that either organism is the cause of the disease they suggest the diphtheroid bacillus may in symbiosis play a part.

H. S. S.

BLACKWATER FEVER.

CONNAL (Andrew). **Figures relating to Blackwater Fever in Nigeria. Part I.**—*West African Med. Jl.* Lagos. 1930. Oct. Vol. 4. No. 2. pp. 32–39.

In this report information has been collected concerning 832 cases of blackwater fever notified in Nigeria between 1899 and 1929. Not any of the histories are complete and in some instances, especially during the earlier years, the data supplied are meagre. Most of the information was obtained from the patients themselves, much has been given by friends and fellow-workers, and some has been collected from Staff Lists and Gazettes. This paper, which constitutes the first part of the report, deals with the amount of quinine taken, and with the length of the interval elapsing between the last doses of the drug and the onset of haemoglobinuria. The patients are divided into three classes, viz., Class A, B and C.—

"*Class* (*a*).—Those who professed to take quinine regularly as a prophylactic measure against malaria.

"*Class* (*b*).—Those who admitted irregularity, such as 'usually daily,' 'occasionally forgetting,' or 'sometimes missing' taking the prophylactic dose of quinine.

"*Class* (*c*).—Those who took no quinine, or seldom or rarely took it, or took it only when they were ill."

Class A contains 130 cases, the dosage was usually 5 grains daily, but there were many exceptions. Connal remarks that although the dosage was regular it could not in all cases be regarded as sufficient for prophylactic purposes; and he adds that absolute regularity was not attained in every case, and that this class undoubtedly contains a number of cases which, had strict regard to the truth been observed by the patient, should properly have come into Class B.

Class B contains 172 cases and it may be accepted that practically in every instance the dose, which was taken irregularly, was one of 5 grains, with an occasional extra 5 grains added to make up for a lapse.

Class C contains 88 cases. Those who "took no quinine" numbered 35, those who took quinine "only when ill" numbered 28, those who took it "rarely" 13, and those who took it "seldom" 8.

Cases are also divisible into groups according to the amount of quinine taken. This and much other information is given in tables which it is impossible to summarize here and which should be consulted in the original by those interested.

Commenting on his statistics Connal states that it may be accepted that at least 70 per cent. of the Europeans resident in Nigeria, as in the other British West African Colonies, took 5 grains of quinine with regularity, usually daily, although on occasions a dose may be missed or the hour taking it altered.

As regards the influence of quinine in the causation or in the precipitation of blackwater fever, it is to be noted that 52 cases are recorded in which no quinine had been administered for a period of at least three days before the appearance of haemoglobinuria. There is an instance of a patient accustomed to take 2½ grains of quinine daily discarding

the practice for 10 days and then developing blackwater fever. Another patient developed blackwater fever 14 days after the last dose of quinine. In seven cases, including five adult negroes, no quinine whatever had been taken. Twenty-four out of fifty-two had taken no quinine for a period varying between some weeks and 34 months. Of the thirty-eight regular five-grain takers, twenty-six developed haemoglobinuria twelve or more hours after their usual prophylactic dose, and in nine the interval was 24 hours. Turning to the large doses there are instances of blackwater fever supervening after three consecutive doses of 15 grains each, of 5 grains taken four times daily for five successive days, of 10 grains taken twice daily for six successive days, and of 5 grains taken four times daily for eight successive days before haemoglobinuria occurred. Even larger doses have been taken, such as 10 grains, thrice daily for eleven consecutive days before the attack.

It may be accepted that in every instance the disease was typically blackwater fever. The two factors to be discussed are the toxic effect of the malaria parasite and possibly the toxic or toxin-liberating effect of quinine. As has been shown, a considerable number of cases of blackwater fever are not obviously associated with recent quinine. In the majority of cases, however, there is a very definite association. There are two reasons for this: (*a*) prophylactic quinine is in common use; and (*b*) quinine is practically always taken or prescribed in the treatment of fever until it is decided that the fever is not due to malaria. It may be said that the interval between the last dose of quinine and the appearance of haemoglobinuria varies, the dose varies, the total amount of quinine varies, and the possible accumulative effect varies. In fact, if quinine be the precipitant it is sometimes delayed in its action, sometimes rapid; sometimes only minute single or successive doses are required; and sometimes large single or successive doses.

The author considers that these facts may be explained by delayed absorption or it may be that the critical stage in a malarial attack which precedes the lysis of the red blood corpuscles had not been reached, while the earlier doses were being administered. In view of the facts, however, it seems possible to acquit quinine of specific complicity in the production of blackwater fever. It is more fitting to stress that quinine is the greatest safeguard against it, for, by proper quinine treatment, no case of malaria due to the subtertian parasite should proceed to that chronic condition of infection which is the precursor of blackwater fever. [This statement is of little value unless accompanied by a precise definition of what is implied "by proper quinine treatment."] It cannot be denied that in many cases quinine is apparently the immediate cause or precipitant in blackwater fever. Nevertheless, when malarial parasites are present in the blood, quinine must be administered, and if the drug be given cautiously it is more than probable that its definite curative effect far outweighs its causative rôle in blackwater fever. [Here again the author should define the word "cautiously."] It should be emphasized that at a certain stage of chronic subtertian malaria in certain subjects, because of inadequate quinine treatment, a febrile attack which culminates in blackwater fever is inevitable and will ensue whether or not quinine be administered. [It would really be interesting, if not advantageous, if the author would be good enough to state precisely what he regards to be adequate quinine treatment, and adequate quinine prophylactic treatment.] There were 102 deaths in 390 cases. The death-rate is lowest in the

regular quinine takers and highest in those who habitually neglect the prophylactic use of the drug. The following figures are given :—

Regular takers	...	130 cases, 25 deaths, 19·23 per cent.
Irregular takers	...	172 cases, 43 deaths, 25 per cent.
Seldom takers ...	...	88 cases, 34 deaths, 38·62 per cent.

The author concludes by remarking that the effect of quinine during the course of, or after the cessation of, haemoglobinuria will be discussed in a later communication.

W. Y.

i. Lee (S. W. T.). **Report on Blackwater Fever in Uganda for 1929.**—*Uganda Protectorate Ann. Med. & San. Rep. for Year ended December 31st, 1929.* Appendix No. III. pp. 89–94. With 1 chart.

ii. Roberts (C. E.). **Two Cases of Blackwater Fever in Africans.**—*Ibid.* Appendix A. p. 70.

i. During 1929, a total of 113 cases of blackwater fever were reported as having occurred in Uganda. Reports were submitted by Government Medical Officers of 73 cases—10 Europeans, 60 Asiatics, and 3 African natives. From mission doctors and private practitioners 9 cases were reported—1 European, 7 Asiatics, and 1 African native. Twenty-one other cases were reported without details. The mortality amongst 113 cases was 18 (21·9 per cent.) [? 15·9]. In tables information is given regarding the distribution of the cases throughout the Protectorate, the number of cases occurring in each month, the age of the patients, and the length of residence of the Europeans in the tropics. Nineteen of the patients are reported to have had previous attacks of blackwater fever. Seven of the patients are stated to have taken prophylactic quinine regularly, 46 to have taken it irregularly, 7 not to have taken it at all, and in 13 there is no record. Details are given in tabular form of the results of blood examination.

ii. Details are given concerning two cases of blackwater fever in African natives. The first was fatal and was, in fact, only diagnosed at post-mortem examination ; the second patient recovered.

W. Y.

Lee (S. W. T.). **Report on Blackwater Fever in Uganda for 1930.**—*Uganda Protectorate Ann. Med. & San. Rep. for Year ended December 31st, 1930.* Appendix III. pp. 82–87. With 1 chart. [Received 7th September, 1931.]

During 1930, 147 cases of blackwater fever were reported in Uganda, 18 Europeans, 122 Asiatics, and 7 Africans. The mortality amongst the Europeans was 22·2 per cent., amongst the Asiatics 25·4 per cent., and amongst the Africans 14·2 per cent. Details concerning the distribution throughout the Protectorate, the monthly variation over the last six years, race, sex and age, length of residence in the tropics, previous attacks of blackwater fever, quinine prophylaxis, and condition of the blood are given in tables.

W. Y.

SHELLEY (Horace M.). **Blackwater Fever in Nyasaland—An Analysis of Sixty-Seven Cases.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1931. Aug. 8. Vol. 25. No. 2. pp. 129–136. With 2 charts & 1 map in text.

The statistics used in this article were compiled from reports on cases which were submitted to the Nyasaland Government by various medical officers, including the author, during the period 1921–1930. During the period in question there were 50 cases amongst Europeans and 17 amongst Asiatics.

The following summary is given :—

" 1. Malaria is widespread over the whole country, and the incidence of the different species of *Plasmodium*, is as follows :—*P. falciparum* 84 per cent., *P. vivax* 14 per cent., *P. malariae* 2 per cent.

" 2. Anti-malarial measures are unsatisfactory, and this is particularly true for the planter section of the population.

" 3. Blackwater fever has not shown any tendency to increase in proportion with the population.

" 4. No race except the indigenous native is immune from attack.

" 5. Two-thirds of the cases occurred in the highlands of the country where there is a heavy rainfall and high humidity.

" 6. Most of the cases were seen during May, June and July, in the middle of the dry season, when it is so cold that fires are required.

" 7. The prevalence of reported cases of malaria and the incidence of blackwater fever during any given year appear to show no coincidence.

" 8. Most cases of the disease occurred in persons of from 20 to 30 years of age.

" 9. Occupation is of considerable aetiological importance. A striking feature is the absence of the disease in Government officials, and its prevalence in members of the planting community.

" 10. Over 90 per cent. of the patients gave a history of repeated attacks of malaria.

" 11. The susceptibility of an individual to blackwater appears to increase during his first year in the country ; and to diminish again until the sixth year of residence when he again becomes very susceptible.

" 12. The onset of the disease is not always ushered in by a rigor, the presence or absence of which is of little prognostic import.

" 13. No racial differences were noted in the duration of haemoglobinuria.

" 14. Parasites were found in the blood of ten patients only.

" 15. One patient's temperature did not rise above normal throughout the whole of his illness.

" 16. Suppression of urine was the chief complication, and occurred in 14 per cent. of the total number of cases.

" 17. There is no specific treatment for the disease."

W. Y.

STRICKLAND (C.) & CHOWDHURY (K. L.). **Blackwater and Malaria in the Darjeeling Terai.**—126 pp. With 1 chart & 4 folding maps. [13 refs.] 1931. Calcutta : Catholic Orphan Press, 3 & 4, Portuguese Church Street.

The Darjeeling Terai of Northern Bengal, which was the scene of the work here reported upon, is a notoriously malarial and blackwater fever-affected area. An account is given of the physiography of the country, and a summary of the findings regarding the anophelines present, the spleen index, and the parasite index in children. The

spleen index for the whole Terai was 73·6 per cent. amongst 2,221 children ; the parasite index was 47·4 per cent., of which 17·5 per cent. were multiple infections. Of 1,753 slides examined, 27·4 per cent. showed *P. vivax*, 9·5 per cent. *P. malariae*, and 30·8 per cent. *P. falciparum*. Between January, 1918, and March, 1929, the recorded cases of blackwater fever amounted to 85.

The authors gave the following summary of their work :—

" We have concluded that blackwater in the Darjeeling Terai occurs always in persons that have been associated with communities subject to hyperendemic malaria, and the inference to be drawn from this is that a high malaria-infection or inoculation-rate in the individual is a necessary predisposing factor. Keeping this hypothesis in view the comparative freedom of some highly malarious countries seemed to need explanation and such cases we think to be due to a favourable chance distribution in the constituents or sections of these communities of that multi-inoculation rate.

" We have accounted for the chance divergences from an average infection-rate in the community, which we postulate to be necessary for the induction of blackwater in the individual, by the proposition that *funestus*, by reason of special habits, as opposed to those of say the common malaria-carrier *maculatus*, is a particular agent in the case. Manson-Bahr has said that the occurrence of several cases in the same family may not be pure coincidence, but probably may be explained by exposure to a common factor which " has given rise to the term ' blackwater-fever houses ' in certain districts, especially Rhodesia, but these when investigated are proved to be bungalows with exceptionally bad surroundings, and highly malarious." In the Terai that ' common factor ' is, we think, *funestus*.

" On the analogy of the correlation that we found in blackwater gardens between the degree of blackwater incidence and malarial endemicity which was in keeping with general opinion in the matter, we consider that a correlation that we discovered between blackwater and both quartan and benign tertian infection may represent a true picture of a special relationship between these parasites and blackwater. Malignant-tertian infection consistently appeared to have the least influence, but in view of the insistent statements elsewhere to the contrary we are inclined to conclude that the different species have no specific importance, and that, in one country, one species, in another, another, may be concerned. No extensive statistical analysis can we think possibly decide this point, it may only indicate the truth which must be clinched in the clinical laboratory.*

" We have not observed any association between blackwater and any other species of malaria-parasite than those mentioned. The suggestion of another infection superposed on malaria inducing blackwater we have been inclined to disregard on the common ground that it is unwise to look for two diseases in one syndrome.

" In view of the malaria-theory of blackwater we have elucidated some facts that follow logically from the theory. For instance we found a great predisposition to blackwater among some who lived close to masses of highly infected persons, to wit the coolies on the estates.† The condition of a habitation did not appear to have much influence, nor did the proximity of jungle round about : the latter being on all fours with the discovery made in Malaya by the senior writer of this report that jungle is not usually dangerous, as so often believed. We also note here the opinion commonly held by medical officers long resident in the Tea Districts, *viz.*, that the introduction of mosquito-proof houses for the European

---

* The F.M.S. Medical Dept. Annual Reports 1927 and 1928 specifically mention that both *P. vivax* and *P. falciparum* were found in blackwater cases.

† At a furlong distance the chance of a non-cooly habitation becoming stricken with blackwater was 22 : 3 = 88 per cent.

superior staff of the Estates has appeared to be a very important factor in determining a lesser incidence of blackwater in this community.

"A general correspondence in the seasonal incidence of malaria with blackwater, this however being a little later, is further evidence in favour of the malaria-theory.

"Incidentally it shows that lengthy 'incubation' of blackwater is not usual; and that this is so is also proved by the frequent reports of cases in which the first attack has occurred within a few weeks' residence in a country, a circumstance coming within also our purview in the Terai. The evidence then indicates that the hypothetical multi-inoculation of malaria may rapidly give rise to a predisposition to blackwater; a long period of gestation is not necessary.

"With regard to differential racial incidence, the remarkable freedom, comparatively speaking, of the 'cooly' from blackwater under highly malarious conditions, could not be accounted for on the ground that he is an *indigène*, because he is not so, nor on the ground of malarial 'immunity,' as about 11,000 of this class came from the Nepál country high above the malaria-zone, and were notoriously susceptible to malaria. We have suggested then that the cooly, whether of a malaria 'susceptible' caste or malaria-'immune,' is saved from a high malaria inoculation-rate and therefore blackwater, by reason of his habit of fumigating his habitation daily with the smoke of his kitchen fire; or alternatively that his habit of living in close association with his domestic animals may divert some degree of infection from himself.

"On the subject of quinine we have shown that it is mostly those of the population who take quinine that develop blackwater but we have also seen that coolies who take quinine do not suffer from blackwater to the same extent as other races who take quinine, which we ascribe to the lesser predisposition of the cooly to blackwater, as noted immediately above. Quinine is to be regarded as a spark that explodes the malarial multi-inoculation bombshell.

"The fact that in one person blackwater could always be induced by the administration of quinine, as also the cases that occur in England, indicate that once the predisposition through malaria multi-inoculation has been induced it persists and an exciting cause may at any time induce the condition.

"It may be quinine, it may be cold or exposure, or if one may trust to one's memory of a public lecture it may be due to taking a surfeit of ice-creams."

After a short section on malaria, the report closes with certain recommendations for the prevention of blackwater fever and malaria and a lengthy series of tables giving information on such points as spleen-indices and blackwater fever incidence, parasite-indices, mosquitoes, condition of estate houses and surroundings, blackwater case records, blackwater distribution in the Terai, and so forth.

W. Y.

STRICKLAND (C.) & CHOWDHURY (K. L.). **Malaria and Blackwater Fever at Noamundi.**—*Indian Jl. Med. Res.* 1930. Oct. Vol. 18. No. 2. pp. 377–389. With 1 map in text. [3 refs.] [School of Trop. Med. & Hyg., Calcutta.]

In August, 1929, the authors were enabled to make a few observations on some of the conditions associated with blackwater fever and malaria at Noamundi, a railway settlement in the Singhbhum district of Chota

Nagpur and, as a control to these observations, some others in an adjoining valley—that of Betlata, which is the home of the aboriginal Kols.

The following summary is given :—

" The observations that we made in this Noamundi area lend support to the theory evolved by us from the data collected in the Darjeeling Terai that while blackwater is usually associated with hyper-endemic malaria, its irregular distribution, as exemplified by b.w. houses, is due to variations from an average malaria infection-rate leading to a more intense local infection-rate sufficient to induce the condition.

" A spleen-index of any size from 0 to 100 may hypothetically represent an average infection rate per person either sufficient or insufficient to induce b.w. As, however, a spleen-index of 100 per cent. often does not lead to b.w. we must presume that unless the average infection rate is *n* times the minimal rate that can produce this spleen-index b.w. will not arise, but if the necessary rate be attained all the persons in a community will get b.w. As this never occurs we must conclude that an average rate applied to all members of a community never happens. Variations from the average infection-rate of a community lead to more intense infection-rates in some and less intense in others and when the critical infection rate is reached the b.w. prodrome is induced, so that ex-hypothesi if the local variation is sufficient a minimal spleen-index may be associated with b.w., or if the variation from the average is not sufficient even a 100 per cent. spleen-index may not be associated with b.w. It is only a matter of chance.

" In the concrete, at Noamundi what was not a so-called hyper-endemic malaria-rate, viz., 44 per cent., was associated with much b.w.

" The necessary variation in the malaria infection-rate is, as we have concluded for the Terai, the function of the species *A. funestus*. Sufficient variation from an average infection-rate, in itself sufficient to yield a 100 per cent. spleen-index, is not a function of *A. maculatus*. The reason for the difference doubtless lies in a difference in habits, one of which is a certain ' domesticity.' In the Terai we showed that this in *funestus* might be given as 16 times that of *maculatus*.

" At Noamundi we have concluded that *culicifacies* is the agent and it would appear that the variation from the average infection-rate whenever this species is the agent is even greater than in the case of *funestus*, for severe b.w. at Noamundi was associated with the comparatively low spleen-index of 44 per cent. (75 per cent. in the Terai) and this fact is to be explained on the ground of a greater domesticity of *culicifacies* (we made it 30 times that of *maculatus* and about twice that of *funestus*).

" One is then naturally led to wonder whether all the *Myzomyias* have such particularly domestic habits that they are all associated with b.w. *A. jeyporiensis* is the reported carrier of malaria in the Jeypore Hill Tracts.

" The distribution of b.w. among Bengalees as opposed to coolies at Noamundi may be accounted for as in the Terai, on the ground, not of ' malaria immunity,' but that the coolies naturally and constantly fumigate their dwellings. Mr. McGregor conducting the collection of adults for us always found it very difficult to catch anophelines in the coolies' ' bashas '* while he could constantly find large numbers in the superior habitations.

" One may conclude that while most of the superior classes took quinine for malaria, only a small proportion of coolies did so, although this constituted a larger absolute number than the former. Therefore if quinine treatment be an excitant of b.w. it follows that the necessary fragility of the blood is not so prevalent in the cooly, which we have explained above.

W. Y.

---

* Hutments, habitation.

SOROMENHO (L.). **Spirochaetes in the Faeces of Patients with Blackwater Fever.**—*Lancet.* 1930. Nov. 8. pp. 1015–1016. With 1 text fig.

Being impressed with the predominance of biliary symptoms in blackwater fever, the author decided to examine the bile with a view to searching for the cause of the disease. He punctured aseptically the gall bladder of a patient who had died six hours previously of a severe attack of blackwater fever at Tete, Portuguese East Africa. Films of the bile stained with carbol-fuchsin showed innumerable spirochaetes. Supported by this discovery he examined the faeces, blood and urine of the next seven cases of the disease which fell into his hands. Nothing was found in the blood or urine, but in the faeces of every case spirochaetes were found—numerous during the febrile stage and disappearing rapidly as the temperature fell and the patient entered convalescence. Soromenho writes "In the faeces of a few cases (four) of quinine haemoglobinuria (at the beginning indistinguishable by its symptoms from true blackwater fever), I was unable to find any spirochaetes." Neither could he find spirochaetes in 14 white patients suffering from intestinal complaints, but they were present in the faeces of 6 of 23 natives with intestinal troubles.

The spirochaetes in the faeces of the natives were indistinguishable from those in the blackwater fever patients and were apparently *Spirochaeta eurygyrata* or, at least, a very closely allied organism. The author in conclusion enquires whether the spirochaete he has found has any connexion with the aetiology of blackwater fever or is merely a normal saprophyte of human stools. [On the face of it, the latter seems the more probable conclusion.]

W. Y.

MÜHLENS (P.) & KNABE (K.). Ein Fall von Schwarzwasserfieber mit aussergewöhnlich starker Chininüberempfindlichkeit. [**A Case of Blackwater Fever with Unusually Pronounced Quinine Susceptibility.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1931. Feb. Vol. 35. No. 2. pp. 73–81. With 1 folding plate. [Inst. for Ship & Trop. Diseases, Hamburg.]

Since the War but few cases of blackwater fever have been admitted to Hamburg for treatment, and during the last 7 years the authors have only seen 9 cases; one of the patients suffered from diabetes and died, as did also a second from cachexia. The remainder recovered and again became accustomed to quinine.

Among these cases was one of special interest not only because of his remarkable sensitiveness to quinine, but also because it was not until after treatment lasting 5 months that a clinical cure of the malaria and blackwater fever was obtained and the patient had become tolerant of quinine. A very detailed account of this case is given and should be consulted in the original by those interested.

The following are the main facts :—

The patient, a young seaman, took for the first time in 1929, one tablet of quinine as a prophylactic; it was badly borne. On February 2nd, 1930 he had an attack of malaria in West Africa and was given a tablet of plasmochin compound. Again, the drug was badly tolerated and vomited. The patient had further attacks of fever, and when he was admitted to the Institute for Tropical Diseases in Hamburg, the blood contained numerous *P. falciparum*. He was again given a tablet of quinine plasmochin (quinine 0·3 gm., plasmochin 0·01 gm.); this was followed by a

severe attack of blackwater fever. The authors draw attention to the fact that in this case there was no prolonged sojourn in the tropics, no prolonged tropical malarial infection, and no long or irregular prophylactic quinine. In fact, from the very beginning the patient had shown definite quinine idiosyncrasy.

It was found impossible to accustom the patient to quinine. Even the smallest doses, e.g. 0·05 gm. of quinine urethane produced haemoglobinuria. This was the more unfortunate, as *P. falciparum* did not disappear from the peripheral blood and the patient had repeated attacks of malaria. On account of the malaria, repeated efforts were made to accustom the patient to quinine, and the drug was given in combination with other medicaments, such as cholesterin, neosalvarsan, etc. Each attempt, however, was followed by blackwater. In all, the patient had nine attacks of blackwater and numerous paroxysms of malaria. The result was he became exceedingly ill and debilitated.

In view of the impossibility of employing quinine, plasmochin alone was tried. This drug was well tolerated and as much as 0·02 gm. was given daily for 21 consecutive days. In all, during the six months, the patient received 4·755 gm. of plasmochin, which appears to be the greatest amount ever given to a patient without any ill effects. Unfortunately, however, these prolonged courses of plasmochin alone did not result in the disappearance of rings from the peripheral blood for more than a short period. In contrast, however, it is noted that crescents were never found whilst the patient was taking plasmochin, but that they appeared once 7 days after, and on two occasions 10 days after, the cessation of plasmochin. On a further administration of plasmochin crescents again disappeared. In this case, it is clear, therefore, that plasmochin alone did not suffice to clear the blood of schizonts.

The quinine double salt, beitusan (0·075 gm. quinine, together with calcium lactate) was tried on April 15th. The patient reacted with high fever, and after three similar doses the next day he had an attack of blackwater. On April 23rd a single dose of beitusan again produced high fever with severe general symptoms, but not haemoglobinuria.

After a 21-day course of plasmochin, several neosalvarsan injections were given, and between May 26th and June 18th, in addition to repeated doses of plasmochin, an intramuscular injection of 5 cc. of splenotrat (Nordmarkwerke, Hamburg) was given every second day, and on the intervening days spleen and liver were given by the mouth. On June 18th, beitusan was again commenced and it was now found possible gradually to accustom the patient to this drug until daily doses of 0·5 gm. were tolerated. On July 2nd after a dose of 0·55 gm. of beitusan, the patient had a slight attack of blackwater fever. Up to July 8th, he was given in all 18 injections of splenotrat. Ultimately, it was found possible with the aid of beitusan and plasmochin to cure him, and he has remained free from parasites since July 14th. The last examination was on November 29th, when the blood was found to be negative and the spleen and liver to be normal.

The authors consider that the feeding with spleen and the injections of splenotrat may have had something to do with the development of quinine tolerance in this patient and consider that further observations on these lines should be made. W. Y.

LEMIERRE (A.) & RUDOLF (Maurice). Sur un cas mortel de fièvre bilieuse hémoglobinurique. [**A Fatal Case of Blackwater.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1931. May 11. Year 47. 3rd Ser. No. 15. pp. 721–729. With 4 text figs. [1 ref.]

An account is given of a patient who was admitted to hospital in Paris during the evening of May 15th, 1929, suffering from a severe

attack of blackwater fever. When seen by the authors the next morning the patient was moribund; there was marked icterus, the liver was normal, and the spleen was enlarged and easily palpable. The patient died at 1.30 p.m. The urine contained haemoglobin, a few leucocytes, but no red cells. The blood count gave: Erythrocytes, 870,000, and leucocytes 18,900; no malarial parasites were found.

This brief clinical account is followed by a detailed description of the pathological findings at the autopsy; the most interesting were those of the liver and kidneys.

Liver. There was a remarkable integrity of the hepatic parenchyma. There was no dislocation of the cells, they appeared normal, and there was no fatty degeneration. There was no vascular distension, but all the capillaries contained, in addition to more or less normal red cells, an abundance of haemoglobinic granules. These granules, so far as their size and staining affinities were concerned, appeared to be identical with those found in the renal tubules. The portal spaces were normal without inflammatory changes. Staining by Levaditi's method failed to reveal spirochaetes; and no malarial parasites were found in sections.

Kidneys. On the whole, the kidney structure was remarkably well preserved. All the tubules (the secretory and excretory) were full of haematinic granules. For the most part the tubules appeared intact. Only here and there was there evidence of fatty degeneration. There was no renal sclerosis or capillary congestion. In places, however, the convoluted tubules showed desquamation. In the pyramidal portion were plugs, partly purely haemoglobinic in nature and partly cellulo-haemoglobinic.

[These renal appearances have, of course, frequently been described in blackwater fever, and also by the reviewer in babesia infection and in experimentally produced haemoglobinuria. The observation of similar granules in the hepatic capillaries is interesting.]

W. Y.

BLANCHARD (M.). Sur la pathogénie de l'hémoglobinurie dans la fièvre bilieuse hémoglobinurique. [**The Origin of Haemoglobinuria in Blackwater.**]—*Bull. Soc. Path. Exot.* 1931. June 10. Vol. 24. No. 6. pp. 473–475. [2 refs.]

The author refers to the paper of LEMIERRE and RUDOLF [above] and remarks that it is very rare to find so complete an account of the pathological findings in this disease and at the same time one which has so great an interest for a conception of the pathogenesis of the haemoglobinuria. He mentions the two theories concerning the site of haemolysis in blackwater fever, viz., the renal and the vascular. The chief difficulty in accepting the latter theory is the fact that many observers have failed to find haemoglobinaemia. [In the reviewer's opinion this is because these observers have failed to examine the blood at the proper time, or because their technique was inadequate. The reviewer has invariably discovered definite evidence of haemoglobinaemia in the many cases he has examined during a blackwater fever paroxysm.]

The mechanism of a renal haemolysis would be as follows: Under the influence of a vaso-constriction produced by the rigor, which occurs at the commencement of every case, there is produced a renal congestion with small intraglomerular haemorrhages; the red cells are then lysed

either in the kidney by haemolysis or in the urine owing to the hypotonicity of this fluid [the reviewer has frequently shown that the urine is not hypotonic in blackwater fever.]

The haemolysis in this case was evidently vascular because the granules of haemoglobin were present both in the liver and in the kidneys.

W. Y.

PENINGTON (Raymond G.). **Blackwater Fever with Hyperpyrexia in a New Guinea Native.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1931. Aug. 8. Vol. 25. No. 2. pp. 137–140. With 1 chart.

Despite the high rate of malignant tertian malaria among the natives of New Guinea, blackwater fever is so rare that the author considered that it was worth while giving a detailed account of a case which came under his care. He draws attention to the following points of interest in the case :—

" (1) Blackwater fever occurring in a full-blooded native.

" (2) The long period of haemoglobinuria with subsequent recovery : *viz.*, eight days, with two recurrences when taking quinine, the first lasting twelve hours, the second, eight hours.

" (3) The comparatively large quantities of urine passed daily throughout the illness.

" (4) The occurrence of frequent rigors, daily or more often, during and subsequent to haemoglobinuria, associated with an absence of malaria parasites in blood films.

" (5) The comparatively slow pulse-rate throughout the disease."

UJLAKI (P.). Beitrag zur Therapie des Schwarzwasserfiebers. [**The Therapy of Blackwater Fever.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1930. Dec. Vol. 34. No. 12. pp. 625–629. [7 refs.]

The paper commences with various speculations regarding the etiology of blackwater fever. The author believes that certain people have a predisposition to blackwater in that in them there exists a constitutional lability of the combination of haemoglobin with the red cells. He considers furthermore that the immediate cause of the disease is a disturbed liver function. This disturbed liver function is due to prolonged malaria infection. He added the washed red cells of a blackwater fever patient to the serum of an untreated case of malaria. No haemolysis occurred. When, however, a piece of liver from a patient who died from blackwater fever was added to the mixture, haemolysis took place. He considers that this observation, which, by the way, he has not had an opportunity of repeating, confirms his hypothesis, in that in his test tube he had all three factors necessary for the production of haemolysis, viz., the defective red cells of a blackwater fever patient, the liver factor from a dead case of blackwater, and the plasmodium-rich serum of a malaria patient.

On the basis of this hypothesis, the author has devised a method of treating blackwater, which consists essentially in the administration of glucose by the mouth and insulin injections, with a view to supporting the liver function. In order to counteract the haemolysis he gives injections of auto-serum. Quinine is only given when parasites are present in the blood.

W. Y.

MATHIEU. Les injections d'huile cholestérinée dans le traitement de la fièvre bilieuse hémoglobinurique. [**Injections of Cholesterinated Oil in the Treatment of Blackwater.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1931. Jan. Vol. 9. No. 1. pp. 28–50. [Luang Prabang Hosp., Luang Prabang.]

Dr. OTT sent to the author at Luang Prabang (Laos) some ampoules of cholesterinated oil, and asked him to try the drug in cases of blackwater fever. Details are given of 14 cases so treated. In only one was the issue fatal and in this death appeared to be due rather to malaria than to blackwater fever. The other thirteen cases, some of which were extremely severe, all recovered. The author remarks "that the haemoglobinuria ceased rapidly, thanks to injections of cholesterin in doses of 1 gm. per day."

W. Y.

AMIGUES (M.). Deux cas de bilieuse hémoglobinurique traités par le sérum médical de Normet, avec résultats très favorables. [**Two Cases of Blackwater treated with Normet's Serum, with Benefit.**]—*Bull. Soc. Path. Exot.* 1930. Nov. 12. Vol. 23. No. 9. pp. 999–1000.

Details are given of the treatment of two severe cases of blackwater fever with polycitrated serum (medical serum of Normet). Both cases recovered rapidly and the author believes that his treatment was in some measure responsible.

W. Y.

TALEC. Observation d'un cas de fièvre bilieuse hémoglobinurique. [**A Case of Blackwater Fever.**]—*Ann. de Méd. et de Pharm. Colon.* 1930. Apr.-May-June. Vol. 28. No. 2. pp. 249–254.

A clinical account is given of a case of blackwater fever, in which death occurred from acute anaemia about a week after the cessation of haemoglobinuria, notwithstanding several transfusions of blood and the administration of many other remedies.

W. Y.

GILLISPIE (A. M.). **Report of a Case of Blackwater Fever in a Full-Blooded African Boy.**—*Gold Coast Rep. on Med. & San. Dept. for Year 1929–30.* Appendix B. pp. 185–191.

A clinical account is given of an attack of blackwater in an African native.

W. Y.

REVIEWS AND NOTICES.

KHALIL (Mohamed). **The Specific Treatment of Human Schistosomiasis (Bilharziasis) with Special Reference to its Application on a Large Scale. With Notes: Ueber Fuadin (Neo-Antimosan)** [SCHMIDT (Hans)]; **The Physiological Action of the Antimosan Compounds** [HAMMOUDA (M. M.)]; **Ueber die Beeinflussung des Blutkreislaufes durch einige Antimonpräparate** [WEESE (H.)].—*Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* 1931. Vol. 35. No. 2. pp. 1–128 (105–232). With 14 figs.

Since the war, considerable activity has taken place in investigating the specific therapy of bilharziasis and a large body of literature has accumulated around the subject. In Egypt, where 10 out of its 15 million inhabitants suffer from the disease, these investigations have been especially active; not only have various drugs been tested, but mass treatment of large numbers of patients has been carried out. Professor Khalil, in preparing this monograph on the specific chemotherapy of the disease, has drawn on the results of these treatment campaigns in addition to reviewing all the literature on the subject as far as it was available. The monograph is divided into six sections. The first, a short section, deals with the older non-specific treatment; the second with emetine; the third and fourth with the simpler and with the more complex antimony compounds. The fifth treats of the excretion of antimony from the human body, while the last discusses the pharmacological action of the complex antimony compounds on the circulation and respiration.

Emetine, he holds, is very effective when given in intravenous daily doses, but is not entirely free from danger; its use in Egypt is limited to children and fat patients, to cases of intestinal bilharziasis complicated with amoebic dysentery, or where there is intolerance to tartar emetic or the other antimony preparations. Tartar emetic is the drug in most frequent use, and as over 300,000 cases are treated annually, its technique and disadvantages are fairly well understood and are described in detail. Its more important contraindications are nephritis, heart failure, jaundice, fever or cases of chronic bilharziasis not discharging living ova. Various complex antimony salts have been tried out, the most important being "Neoantimosan" or "Fuadin" which appears to be even more effective than tartar emetic. The duration of the treatment is ten days shorter; more cases can be treated by the same staff and there is an absence of local complications. On the other hand, it is more expensive and in certain cases causes bradycardia.

Pharmacologically, antimony appears to be a cumulative drug which is slowly excreted by the kidney; while the complex compounds, such as fuadin, have hardly any effect on the heart, blood-pressure, respiration or the intestinal movements.

The monograph, which although published in Germany is mostly written in English, contains an extensive bibliography and should prove of great value to the tropical clinician and health official.

T. W. M. Cameron.